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(57) Abstract

Tricyclic heteronaphthoquinone derivatives, that have antineoplastic activity, are disclosed, together with processes for their synthesis. Some of these anti-neoplastics compounds have a saccharide moiety. Some members of this structurally distinct group exhibit activity against multiple drug resistant cancer cells.

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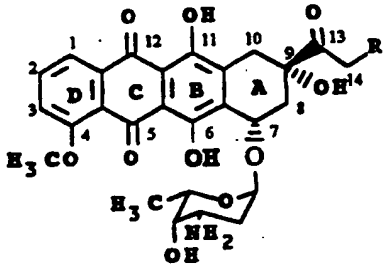
ANTINEOPLASTIC HETERONAPHTHOQUINONES

This invention relates to heterocyclic naphthoquinone derivatives, to processes and to intermediates for preparing these derivatives, to pharmaceutical compositions containing them and to the use of these derivatives as antitumor agents in mammals.

BACKGROUND OF THE INVENTION

Anthracycline antibiotics including doxorubicin and daunorubicin are important chemotherapeutic agents in the treatment of a broad spectrum of neoplastic conditions. While daunorubicin (1) is clinically used mainly against acute childhood and adult leukemias, doxorubicin (2), also known as adriamycin, has the widest spectrum of antitumor activity of all chemotherapeutic agents (Weiss, R.B., Sarosy, G., Clagett-Carr, K., Russo, M. and Leyland-Jones, B., Cancer Chemother. Pharmacol., 18, 185-197, 1986; Arcamone, F., Doxorubicin, Academic Press, New York, 1980).



(1) daunorubicin R = H
(2) doxorubicin R = OH

The usefulness of known anthracycline antibiotics is compromised by dose limiting toxicities such as myelosuppression (Crooke, S.K., Anthracyclines; Current Status and New Developments, Academic Press, N.Y. 1980) and cardiotoxicity (Olson, R.D. et al, Proc. Natl. Acad. Sci., USA 85 3585-3589, 1988 and references therein) as well as the resistance from treated tumors (Minnaugh, E.G. et al, Cancer Research, 49, 8-15, 1989; McGrath, T. et al, Biochemical Pharmacology, 38 497-501, 1989). In view of the proven effectiveness of known anthracyclines in the treatment of cancer, efforts have been undertaken to develop anthracycline analogs with either an improved therapeutic index or with reduced cross-resistance.

Several thousand anthracycline derivatives have been obtained either from streptomyces biosynthesis or via the semisynthetic modification of known natural anthracycline antibiotics (Arcamone, F., Doxorubicin, Academic Press, N.Y. 1980; Thomson, R.H., Naturally Occurring Quinones III: Recent Advances, Chapman and Hall, New York 1987; Anthracyclines: Current Status and New Developments, Academic Press, New York, 1980; Brown, J.R. and Iman, S.H., Recent Studies on Doxorubicin and its Analogues, Prog. Med. Chem. 21 170-236, 1984; Brown, J.R. Adriamycin and Related Anthracycline Antibiotics, Prog. Med. Chem., 15, 125-164, 1978). The majority of known anthracyclines show two types of structural differences: (i) the substitution pattern of the aglycone tetracyclic ring system, and (ii) the structure and number of glycosides attached at C-7 or C-10 (doxorubicin numbering). Some examples of the structural diversity of anthracycline antibiotics are:

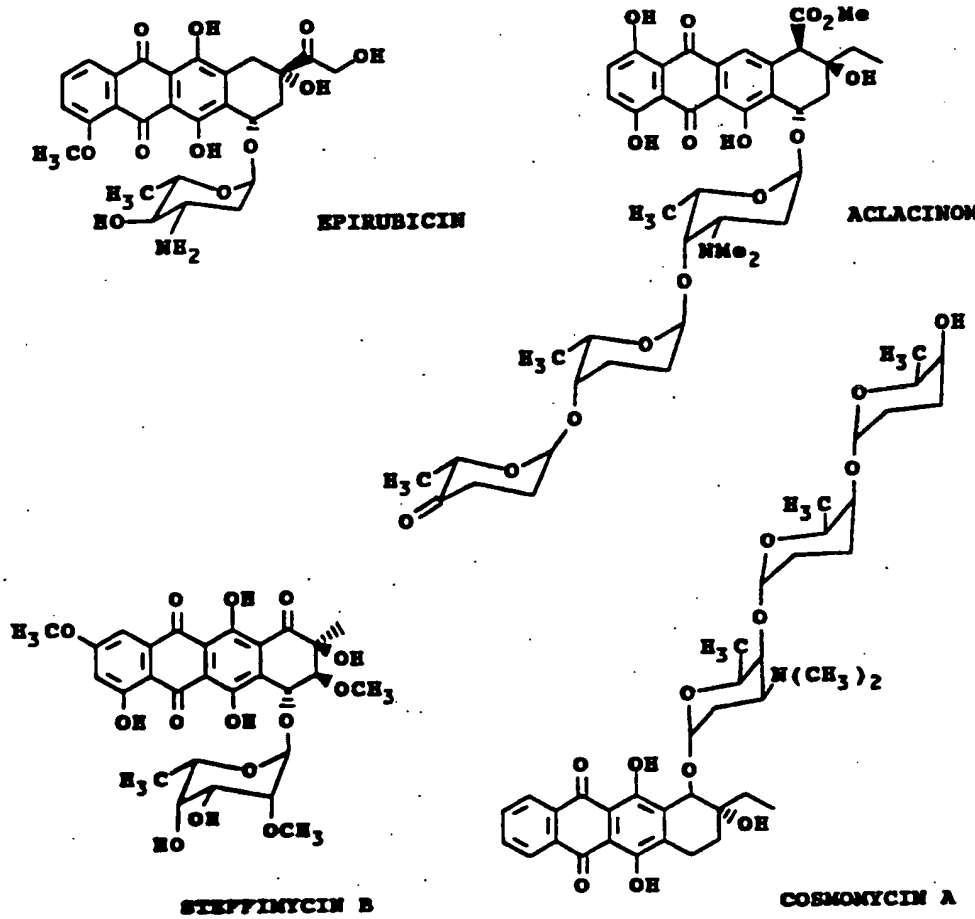
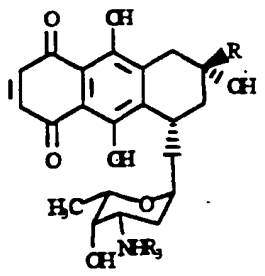


FIG. 1

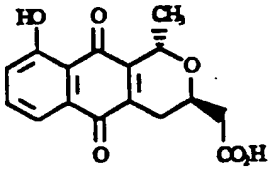
Tricyclic variants (3) of daunorubicin have been reported to possess antitumor activity (EPA 91202015.3)



R is $COCH_3$ or C_CH or C_C-$Si(CH_3)_3$

R_3 is H or $COCF_3$

Pyranonaphthoquinones such as nanaomycin A (4) and kalafungin (5) occur naturally and show potent antibacterial as well as antifungal activity (Moore, H.W. and Czerniak, R., Medicinal Research Reviews, 1(3), 249-280, 1981 and references therein).



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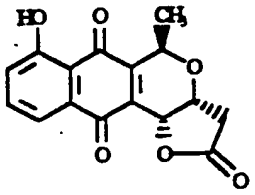

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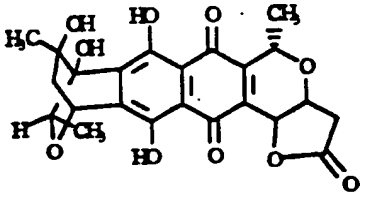

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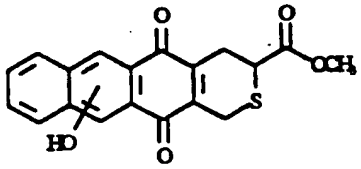
Granaticin (6) has been reported to show antitumor activity (Chang, C.J., Floss, H.G., Soong, P.l and Chang, C.T., J. Antibiot., 28, 156, 1975). More recently thiopyranoanthraquinone (7) and pyranoanthraquinone (8) were found to possess antitumor activity (PCT, CA9100208). In contrast antitumor activity of other 9-oxa-heteroanthracylines such as (9), (10), and (11) was not significant (Heterocycles, 26 (2), 341-5, 1987; Heterocycles 26 (4), 879-82, 1987).



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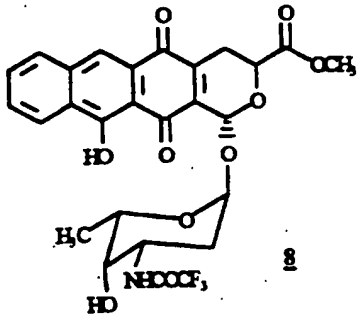

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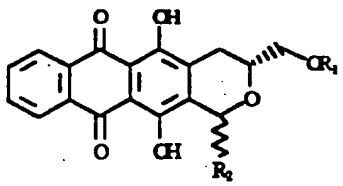
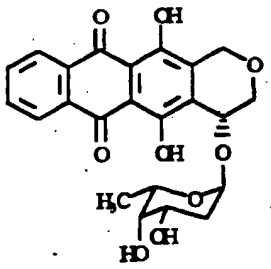




9 R_1= H; R_2= H, CH_3

10 R_1= Sugar, R_2= H, CH_3

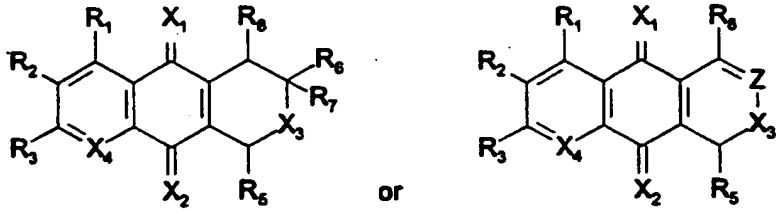
11

DESCRIPTION OF THE INVENTION

The present invention provides heteronaphthoquinones which are structurally distinguished from prior art compounds.

More specifically, the compounds of the present invention are structurally distinguished from the prior art compounds by having a tricyclic heteronaphthoquinone moiety fused to a hydroxyl group or alternatively to a sugar moiety. This structurally distinct class of compounds exhibits therapeutic activity, in particular anticancer and antitumor activity. Some of the compounds are active against certain doxorubicin-resistant tumor cells, and are more potent in some cases than the corresponding tetracyclic heteroanthracycline compound.

In one aspect of the invention, there is provided a compound of the formula (12):



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wherein

X_1 and X_2 are independently selected from the group consisting of

O, S, and N(R), wherein R is selected from the group consisting of hydrogen, hydroxyl, C_{1-16} alkyl, C_{1-16} acyl and C_{1-16} alkylamine.

X_3 is selected from the group consisting of O, S, SO, SO_2, and NR, wherein R is selected from the group consisting of hydroxyl,

C_{1-16} acyl, C_{1-16} alkyl, C_{1-16} aryl, C_{1-16} haloacyl, and hydrogen.

X_4 is selected from the group consisting of C-Q, nitrogen, and NO.

R_1, R_2, R_3, and Q are independently selected from the group consisting of hydrogen, hydroxyl, C_{1-16} alkyl, C_{1-16} alkoxyl, C_{3-8} cycloalkyl, tosyl, mesylate, acetate optionally substituted with a C_{1-8} alkyl, triflate, trifluoroacetate, halogen, nitro, cyano, C_{1-16} acyl, C_{1-16} arylacyl, aminoalkylaminoalcohol of formula $NH(CH_2)_nNH(CH_2)_mOH$ wherein n and m are independently 1 to 4, aminoalkylaminoalkylhalide of formula $NH(CH_2)_nNH(CH_2)_mX$ wherein n and m are independently 1 to 4 and X is a halogen,

amino, which may be unsubstituted or mono or di-substituted by C_{1-8} alkyl, C_{3-8} cycloalkyl, C_{1-8} acyl, trifluoroacyl, C_{7-18} aralkyl and C_{6-18} aryl; C_{2-8} alkenyl, and C_{2-8} alkynyl,

haloalkylnitrosoureido of the formula $NH(CO)N(NO)(CH_2)_n CH_2X$, wherein n is 0 to 4 and X is a halogen, and

-$NH(CH_2)$n N R* R** wherein n is 1 to 6, R* and R** are independently selected from hydrogen, C_{1-8} alkyl, C_{6-18} aryl, C_{7-18} aralkyl, C_{1-8} acyl, and trifluoroacyl,

a group of the formula -O-C(R)=O wherein R is selected from the group consisting of hydrogen, C_{1-16} alkyl, C_{3-8} cycloalkyl, C_{2-12} alkoxyalkyl, C_{7-18} aralkyl, C_{7-18} araloxyalkyl, C_{7-18} aryloxyalkyl and C_{6-18} aryl.

Z is one of C-R_6 or C-R_7.

R_6 is selected from the group consisting of C_{1-16} hydroxime, C_{6-18} hydrazone, C_{1-16} hydroxyalkyl, hydrogen, C_{6-18} aryl, C_{7-18} aryloxyalkyl, C_{7-18} araloxyalkyl, phenyl, C_{1-16} alkyl, acetoxy, C_{1-16} dihydroxyalkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-8} cycloalkyl, squaric acid, C_{1-16} alkyl squarate, amino, cyano, dimethylphosphonato, phenyl sulfone, C_{1-8} aryl sulfone, and

C_{1-8} acetyl, agroup of the formula -C(R) = X* wherein X is selected from the group consisting of two hydrogens, one hydrogen and R* is selected from a C1-8 alkyl, C2-8 alkenyl, C7-18 aralkyl, and O, or its dioxolane or dioxane or dialkoxy C1-8 ketal, and wherein R is selected from the group consisting of hydrogen, C_{1-16} alkyl, C_{1-8} thioalkyl, C_{3-8} cycloalkyl, C_{6-18} aryl, C_{7-18} aralkyl, fluoromethyl, difluoromethyl, C_{1-8} hydroxyalkyl, C_{2-16} alkene, squaric acid, C_{2-16} alkyne, C_{1-8} thioalkyl, C_{6-18} thioaryl, C_{1-4} alkyl squarate, C_{2-8} alkoxyalkyl, C_{6-18} araloxyalkyl, C_{2-18} acyloxyalkyl, C_{1-8} alkoxy, hydroxy, acetoxy methyl, bromomethyl, C_{1-8} aceto, amino which may be unsubstituted or mono- or di-substituted by hydrogen, C_{1-8} alkyl, C_{3-8} cycloalkyl, C_{1-8} acyl, trifluoroacyl, C_{7-18} aralkyl, C_{6-18} aryl,

a group of the formula -CHR* R**, wherein R* and R** are independently selected from the group consisting of C_{1-8} alkyl, hydrogen, PO $(OR)_2$ wherein R is selected from the group consisting of hydrogen, C_{1-8} alkyl, C_{1-8} acyl, C_{6-18} aryl, C_{7-18} aralkyl, and

a group of the formula -$(CH_2)_n$Z* wherein n is O to 7 and Z* is from the group consisting of hydrogen, C_{1-8} acyl, C_{6-18} aryl, C_{7-18} aralkyl, pyrolone, and a 5 or 6 membered aromatic or non-aromatic heterocycle containing one or more heteroatoms selected from the group consisting of O, S, N, SO, SO_2, P, PO and NR wherein R is selected from the group consisting of

hydrogen, hydroxyl, C_{1-8} acyl, C_{1-4} alkyl and C_{6-12} aryl;

said heterocycle being optionally substituted with one or more halogens, hydroxy, C_{6-18} aryl sulfone, C_{1-16} alkoxy, C_{1-16} alkyl, nitro, C_{1-16} hydroxyalkyl,

amino, which may be unsubstituted or mono- or di-substituted by C_{1-8} alkyl, C_{3-8} cycloalkyl, C_{1-8} acyl, trifluoroacyl, C_{7-18} aralkyl, C_{6-18} aryl, C_{2-8} alkenyl, C_{2-8} alkynyl and hydroxy.

Z^* can also be a group of the formula $-NR^*R^{**}$ wherein R^* and R^{**} are independently selected from the group consisting of hydrogen, C_{1-8} alkyl, C_{1-8} acyl, C_{6-18} aryl, C_{7-18} aralkyl, C_{1-8} haloalkyl, C_{1-8} hydroxyalkyl, C_{1-8} alkoxyalkyl, C_{1-8} acyloxyalkyl, C_{6-12} araloxyalkyl, and a group of formula $-CO(CH_2)_n C(PO(OR)_2)_2$ wherein n is 1 to 4 and R is hydrogen or C_{1-8} alkyl; and a naturally occurring amino acid;

a group of the formula -C(OR)=0, where R is selected from the group consisting of hydrogen, C_{1-16} alkyl, C_{3-8} cycloalkyl, C_{1-8} hydroxyalkyl, C_{1-8} alkoxyalkyl, C_{7-18} aryloxyalkyl, C_{6-18} araloxyalkyl, C_{6-18} aryl and C_{7-18} aralkyl;

a group of the formula $-(CH_2)_n C(R)=O$, wherein n is 1 to 6 and wherein R is selected from the group consisting of hydrogen, hydroxyl, C_{1-16} alkyl, C_{3-8} cycloalkyl, C_{1-8} hydroxyalkyl, C_{2-8} alkoxyalkyl, C_{1-8} alkoxy, C_{7-18} aryloxyalkyl, C_{7-18} araloxyalkyl, C_{6-18} aryl, C_{7-18} aralkyl,

amino which may be unsubstituted, mono- or di-substituted by C_{1-8} alkyl, C_{3-8} cycloalkyl, acyl, trifluoroacyl, C_{2-12} aralkyl, C_{2-12} aryl,

a 5 or 6 membered aromatic or non aromatic heterocycle containing one or more heteroatoms selected from the group consisting of O, S, N, SO, SO_2, P, PO, and NR wherein R is

selected from the group consisting of hydrogen, oxygen, hydroxyl, acyl, C_{1-4} alkyl and aryl, said heterocycle being optionally substituted with one or more halogens, C_{6-18} arylsulfone, hydroxy, C_{1-16} alkoxy, nitro, C_{1-16} alkyl, C_{1-16} hydroxyalkyl, amino which may be unsubstituted or mono- or disubstituted by C_{1-8} alkyl, C_{3-8} cycloalkyl, acyl, trifluoroacyl, aralkyl or aryl; C_{2-8} alkenyl, C_{2-8} alkynyl and hydroxy.

R_7 is selected from the group consisting of hydrogen, C_{1-16} alkyl, halogen, amino, hydroxy, C_{1-16} alkoxy, thiol, cyano, sulfide, acyl of the formula -C(R)=O wherein R is selected from

the group consisting of hydrogen, C_{1-16} alkyl, C_{1-16} alkoxy, C_{3-8} cycloalkyl, C_{1-8} hydroxyalkyl, C_{7-18} araloxyalkyl, C_{2-8} alkoxyalkyl, C_{2-8} acyloxyalkyl, C_{6-12} aryloxyalkyl, squaric acid or squarate, amino which may be unsubstituted or mono- or di-substituted by C_{1-8} alkyl, C_{3-8} cycloalkyl, C_{1-8} acyl, cyano, trifluoroacyl, C_{7-18} aralkyl or C_{6-12} aryl, and a naturally occuring amino acid;

a group of the formula -C(OR)=O wherein R is selected from the group consisting of hydrogen, C_{1-16} alkyl, C_{3-8} cycloalkyl, C_{1-8} hydroxyalkyl, C_{2-8} alkoxyalkyl, C_{7-12} aryloxyalkyl, C_{7-12} araloxyalkyl, C_{6-12} aryl, C_{7-18} aralkyl and C_{1-16} alkenyl.

R_5 and R_8 are independently selected from the group consisting of hydrogen, halogen, hydroxyl, C_{1-16} alkoxyl, C_{1-16} alkyl, C_{2-16} acetylenyl, a group of the formula $-(CH_2)_n-NR^*R^{**}$ wherein n is 1 to 6, and R^* and R^{**} are independently selected from a group consisting of C_{1-8} alkyl, C_{1-4} acyl, C_{3-8} cycloalkyl, hydrogen, C_{2-8} carboalkoxy, C_{2-8} alkene, C_{2-8} alkyne, C_{6-12} aryl, and

$(OCH_2CH(PO(OR)_2)_2$

wherein R is a hydrogen or a C_{1-8} alkyl and wherein n is 0 to 5;

C_{3-8} cycloalkyl, C_{2-16} alkenyl, C_{1-16} alkoxyalkylamino, cyano;

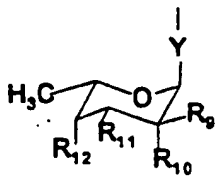
a group of the formula -O-C(R)=O, wherein R is selected from the group consisting of hydrogen, C_{1-16} alkyl, C_{3-8} cycloalkyl, C_{2-8} alkoxyalkyl, and C_{6-12} aryl;

an acyl of the formula -C(R)=O, wherein R is selected from the group consisting of hydrogen, thiol, C_{1-16} thioalkyl, C_{1-16} alkyl, C_{3-8} cycloalkyl, C_{1-8} hydroxyalkyl, C_{2-8} alkoxyalkyl, C_{7-12} araloxyalkyl, C_{2-8} acyloxyalkyl, amino which may be unsubstituted or mono- or di-substituted, and a naturally occurring amino acid or a synthetic amino acid;

a group of the formula -C(OR)=O, wherein R is selected from the group consisting of hydrogen, C_{1-16} alkyl and C_{3-8} cycloalkyl, acosamine, glucosamine, N-chloroethyl-nitrosoureidoglucosamine, 2,6-dideoxyrhamnose, thioglucose, thiodaunosamine, thiol, C_{1-12} thioalkyl, a naturally occuring amino acid or di- and tri-peptides thereof, a group of the formula -Z*-CHRR* wherein Z* is selected from the group consisting of O, CH_2, NR** wherein R** is from the group consisting of hydrogen, C_{1-8} alkyl, C_{2-8} acyl or C_{6-12} aryl,

R and R* are independently selected from the group consisting of hydrogen, C_{1-12} alkyl, C_{6-12} aryl, C_{2-8} dihydroxyalkyl, C_{2-8} alkene, C_{2-8} alkyne, C_{1-8} alkoxy, C_{1-8} alkylamino, C_{3-8} cycloalkyl, C_{2-8} carboalkoxy, a 5 or 6 membered aromatic or non-aromatic heterocycle containing one or more heteroatoms selected from the group consisting of O, S, N, SO, SO_2, P, PO, and NR

wherein R is selected from the group consisting of hydrogen, hydroxyl, C_{1-8} acyl, C_{1-4} alkyl and C_{6-12} aryl, said heterocycle being optionally substituted with one or more halogens, hydroxy, C_{6-18} aryl sulfone, cyano C_{1-16} alkoxy, C_{1-16} alkyl, nitro, C_{1-16} hydroxyalkyl, amino, which may be unsubstituted or mono-or di-substituted by C_{1-8} alkyl, C_{3-8} cycloalkyl, C_{1-8} acyl, trifluoroacyl, C_{7-18} aralkyl, C_{6-18} aryl, C_{2-8} alkenyl, C_{2-8} alkynyl and hydroxy; mono or oligosaccharides of the formula:



wherein Y is selected from the group consisting of oxygen, sulfur, sulfoxide, sulfone, CR*R**, wherein R* and R** are independently selected from the group consisting of hydrogen, C_{1-8} alkyl, and NR wherein R is selected from the group consisting of hydrogen, C_{1-8} alkyl, and C_{1-8} acyl.

R_9 and R_{10} are independently selected from the group consisting of hydrogen, halogen, hydroxy,

acetoxy, C_{1-16} alkoxy, C_{1-16} alkyl, C_{3-8} cycloalkyl, thiol, amino, trifluoroacetamido, chloroethylnitrosoureido, and chloroethylureido.

R_{11} is selected from the group consisting of hydrogen, amino which may be unsubstituted or mono or di-substituted by C_{1-8} alkyl, C_{3-8} cycloalkyl, C_{2-8} acyl, t-butylacyl, C_{1-8} alkoxy, t-butyloxycarbonyl, trifluoroacyl, C_{7-12} aralkyl, C_{6-12} aryl, and a naturally occuring or synthetic amino acid; mono or dibenzylated amino, azido, acylated amino, trifluoroacylated amino, morpholino, cyano substituted morpholino, mono-, di-, tri- or tetra-methoxy substituted morpholino, mono-, di-, tri- or tetra-acetoxy substituted morpholino, hydroxyl, hydrogen, halogen, acetoxy, C_{1-16} alkoxyl, C_{3-8} cycloalkyl, thiol, sulfide; a group of the formula $NH(CH_2)_nCH(OR)_2$ wherein R is selected from the group consisting of C_{1-16} alkyl, C_{1-16} acyl and C_{7-16} aroyl and wherein n is 0 to 5.

chloroalkylnitrosoureido of the formula $NH(CO)N(NO)(CH_2)_nCH_2Cl$ wherein n is 0 to 4, and $NH(CH_2)_2\ OCH_2CH(OA_c)_2$.

R^{12} is selected from the group consisting of hydrogen, hydroxyl or its tetrahydropropyl ether (-OTHP), mesylate, tosylate, halogen, mono or oligosaccharides, C_{1-8} alkoxy, amino, mono or dialkylated amino in which each alkyl contains 1 to 16 carbon atoms, trifluoroacetamido, C_{1-16} alkoxy, C_{3-8} cycloalkyl, C_{2-8} haloalkylacetate, benzoate which may be unsubstituted or substituted with nitro, one of the group consisting of p-nitrobenzoate, acetoxy, trifluoroacetoxy, chloroalkylnitro-soureido of the formula $NH(CO)N(NO)(CH_2)_nCH_2Cl$ wherein n is 0 to 4, and $NH(CH_2)_2\ OCH_2CH(OA_c)_2$.

R5 and R8 can also be independently selected from a 5 or 6 membered aromatic or non-aromatic heterocycle containing one or more heteroatoms, selected from the group consisting of O, S, N, SO, SO_2, P, PO and NR wherein R is selected from the group consisting of hydrogen, hydroxyl, C_{1-8} acyl, C_{1-4} alkyl and C_{6-12} aryl, said heterocycle being optionally substituted with one or more halogens, hydroxy, C_{6-18} aryl sulfone, cyano, C_{1-16} alkoxy, C_{1-16} alkyl, nitro, C_{1-16} hydroxyalkyl, amino, which may be unsubstituted or mono-or di-substituted by C_{1-8} alkyl, C_{3-8} cycloalkyl, C_{1-8} acyl, trifluoroacyl, C_{7-18} aralkyl, C_{6-18} aryl, C_{2-8} alkenyl, C_{2-8} alkynyl and hydroxy.

Preferred compounds of formula (12) are those wherein

X_1 and X_2 are independently selected from the group consisting of

O, S, and NH.

X_3 is selected from the group consisting of O, S, SO, SO_2, NH, and NOH.

X_4 is selected from the group consisting of CQ, N, and NO.

R_1, R_2, R_3, and Q are independently selected from the group consisting of hydrogen, hydroxyl, C_{1-4} alkoxyl, tosyl, triflate, fluorine, chlorine, amino, aminoalkylaminoalcohol of formula $NH(CH_2)_nNH(CH_2)_mOH$ wherein n and m are independently 1 to 3, aminoalkylaminoalkylchloride of formula $NH(CH_2)_nNH(CH_2)_mCl$ where n and m are independently 1 to 3, chloroalkylnitrosoureido of the formula $NH(CO)N(NO)(CH_2)_n\ CH_2\ Cl$, wherein n is 0 to 4, and a group of the formula -O-C(R)=O, wherein R is selected from the group consisting of hydrogen, C_{1-6} alkyl, and aryl;

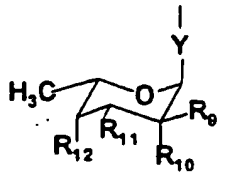
Z is one of C-R_6 or C-R_7.

R_6 is selected from the group consisting of hydrogen, C_{1-8} hydroxyalkyl, C_{1-8} dihydroxyalkyl, squaric acid, C_{1-16} alkylsquarate, C_{1-4} alkyl, acyl of the formula -C(R)=O, wherein R is selected from the group consisting of hydrogen, C_{1-8} alkyl, C_{1-8} hydroxylalkyl, squaric acid, C_{1-4} alkyl squarate, alkoxyalkyl, aminoacetaldehyde diethyl acetal, aminoacetaldehyde diacetoxy acetal, aminopropanol diacetoxy acetal, aminobutanol diacetoxy acetal, aminopentanol diacetoxy acetal, acyloxyalkyl and amino which may be unsubstituted or mono- or di-substituted with C_{1-8} alkyl, C_{3-8} cycloalkyl, acyl, trifluoroacyl, aralkyl or aryl; a group of the formula -C(OR)=O, wherein R is selected from the group consisting of hydrogen, C_{1-8} alkyl, aryl, aralkyl; and a group of the formula $-CH_2C(OR)=O$, wherein R is selected from the group consisting of hydrogen, straight or branched C_{1-8} alkyl, and amino which may be unsubstituted or mono- or di-substituted with C_{1-8} alkyl, C_{3-8} cycloalkyl, acyl, trifluoroacyl, aralkyl, aryl, and a 5 or 6 membered aromatic or non aromatic heterocycle containing one or more heteroatoms selected from the group consisting of O, S, N, NO, NH; said heterocycle being optionally substituted with one or more halogen, hydroxy, C_{1-8} alkoxy, C_{1-8} alkyl, C_{1-8} hydroxyalkyl, amino which may be unsubstituted or mono- or disubstituted by C_{1-4} alkyl, C_{3-5} cycloalkyl, acyl, trifluoroacyl, aryl, and hydroxy;

R_7 is selected from the group consisting of hydrogen, fluorine, C_{1-4} alkyl, C_{1-4} alkoxy, cyano acyl of the formula -C(R)=0 where R is selected from the group consisting of hydrogen, C_{1-8} alkyl, hydroxyalkyl, acyloxyalkyl,

amino, cyano, a group of the formula -C(OR)=0, wherein R is selected from the group consisting of hydrogen, C_{1-8} alkyl, aryl, C_{1-8} alkenyl;

R_5 and R_8 are independently selected from the group consisting of hydrogen, halogen, hydroxyl, C_{1-8} alkoxy, C_{2-8} acetylenyl, C_{2-8} alkenyl, cyano, a group of the formula -O-C(R)=O, wherein R is selected from the group consisting of hydrogen and C_{1-8} alkyl; acyl of the formula -C(R)=0, wherein R is selected from the group consisting of hydrogen, thiol, C_{1-8} alkyl, hydroxyalkyl, amino; a group of the formula -C(OR)=O, wherein R is selected from the group consisting of hydrogen and C_{1-8} alkyl, glucosamine, and a saccharide of formula:



wherein Y is selected from the group consisting of oxygen, sulfur, and CHR wherein R is hydrogen or C_{1-4} alkyl,

R_9 and R_{10} are independently selected from the group consisting of hydrogen, amino, fluorine, chlorine, trifluoroacetamido and hydroxyl;

R_{11} is selected from the group consisting of amino which may be unsubstituted or mono- or di-substituted with C_{1-8} acetoxy alkyl, C_{3-8} cycloalkyl, acyl, trifluoroacyl, aralkyl and aryl; morpholino, azido, cyano substituted morpholino, mono-, di-, tri-, or tetra-methoxy substituted morpholino, hydroxyl, mono or dialkylated amino with 1 to 16 carbons, C_{1-8} alkoxyl, a group of the formula $NH(CH_2)_nCH(OR)_2$ wherein R is independently selected from a group consisting of C_{1-8} alkyl, C_{1-8} acyl and C_{7-12} aroyl and wherein n is 1 to 5; chloroalkylnitrosoureido of the formula $NH(CO)N(NO)(CH_2)_nCH_2Cl$ wherein n is 0 to 4, $NH(CH_2)_2\ OCH_2CH(OA_c)_2$ fluorine;

R_{12} is selected from the group consisting of hydroxyl or its tetrahydropyranyl ether, halogen, mono or oligosaccharide selected from the group consisting of rhodosamine, cinerulose-B, L-cinerulose, D-cinerulose, cinerulose A, amicetose, aculose, rednose, rhodinose, 2-deoxyfucose, daunosamine, trifluoroacetyl-daunosamine, amino, trifluoroacetamido, mono or dimethylated amino, C_{1-8} alkoxy, benzoate, p-nitrobenzoate, chloroalkyl-nitrosourea, acetoxy and trifluoroacetoxy.

More preferred compounds of formula (12) are those wherein

X_1 and X_2 are independently selected from the group consisting of
0 and NH;

X_3 is selected from the group consisting of 0, S and S0.

X_4 is selected from the group consisting of CQ and N.

R_1, R_2, R_3, and Q are independently selected from the group consisting of hydrogen, hydroxy, methoxy, halogen, amino-ethylaminoethanol, aminoethylaminoethylchloride, chloroalkyl-nitrosoureido of the formula $NH(CO)N(NO)(CH_2)_nCH_2Cl$ wherein n is 0 to 2; amino, and
fluorine.

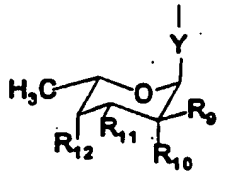
Z is one of C-R_6 or C-R_7.

R_6 is selected from the group consisting of C_{1-4} hydroxime, C_{6-10} hydrazone, C_{1-4} alkyl, C_{1-4} hydroxyalkyl, phenyl, C_{1-4} dihydroxyalkyl, a group of the formula -C(R)=X, wherein X is selected from the group of hydrogen, and O, and wherein R is selected from the group consisting of C_{1-4} alkyl, hydroxymethyl, hydrogen, acyloxymethyl, C_{2-4} alkenyl, C_{2-4} actylyl, C_{1-4} alkoxy, hydroxy, C_{1-4} aceto, amino which may be unsubstituted or mono- or di-substituted by hydrogen, C_{1-4} alkyl, C_{1-4} acyl, trifluoroacyl, and a group of the formula -CHR*R** wherein R* and R** are independently selected from a group consisting of C_{1-4} alkyl, hydrogen, C_{1-4} acyl, a group of the formula $-(CH_2)_nZ^*$ wherein n is 0 to 3 and Z* is a hydrogen, or C_{1-4} acyl, a 5 or 6 membered aromatic or non-aromatic heterocycle containing one or more heteroatoms selected from the group consisting of O and N, said heterocycle being optionally substituted with one or more fluorines, hydroxy, C_{1-4} alkoxy, C_{1-4} alkyl, and amino which may be unsubstituted, mono-or di-substituted by a C_{1-4} alkyl, C_{1-4} acyl, trifluoroacyl and C_{2-4} alkynyl, Z* can also be a group of the formula -NR*R** wherein R* and R** are independently selected from the group consisting of hydrogen, C_{1-4} alkyl, and C_{1-4} acyl;
a group of the formula -C(OR)=O, wherein R is selected from the group consisting of hydrogen, C_{1-4} alkyl; a group of the formula $-(CH_2)_nC(R)=O$, wherein n is 1 to 3 and R is selected from the group consisting of hydrogen, hydroxy, C_{1-4} alkoxy, C_{1-4} alkyl, C_{1-4} hydroxyalkyl, amino, dimethylamino; a

5 or 6 membered aromatic or non aromatic heterocycle containing one or more heteroatoms selected from the group consisting of O, S, N, NO, NH said heterocycle being optionally substituted with one or more halogens, hydroxy, C_{1-4} alkoxy, C_{1-4} alkyl, C_{1-4} hydroxyalkyl, amino which may be unsubstituted or mono-or disubstituted by methyl, cyclopropyl, acyl, and hydroxy.

R_7 is selected from the group consisting of hydrogen, fluorine, methyl, methoxy, cyano, acyl of the formula -C(R)=O, wherein R is selected from the group consisting of hydrogen, C_{1-5} alkyl, C_{1-4} hydroxyalkyl, amino, cyano, a group of the formula -C(OR)=O, wherein R is selected from the group consisting of hydrogen, C_{1-5} alkyl, aryl, and C_{1-4} alkenyl:

R_5 and R_8 are independently selected from the group consisting of hydrogen, halogen, hydroxy, C_{1-4} alkoxy, C_{1-6} alkyl, C_{2-4} alkene,a group of the formula $-(CH_2)_n NR^*,R^{**}$ wherein n is 1 to 4 and R* and R** are independently selected from the group consisting of hydrogen, C_{1-5} alkyl, C_{1-4} acyl; acosamine, 2,6-dideoxyrhamnose, thiodaunosamine, C_{1-5} thioalkyl, a naturally occurring amino acid or dipeptides thereof, a group of the formula -Z*-CHRR* wherein Z* is selected from the group consisting of O, CH_2 and NR** wherein R** is selected from the group consisting of hydrogen, C_{1-4} alkyl and C_{2-4} acyl, and wherein R and R* are independently selected from the group consisting of hydrogen, C_{1-4} alkyl, C_{2-4} alkene, C_{1-5} alkylamino, a 5 or 6 membered aromatic or non-aromatic heterocycle containing one or two heteroatoms selected from the group consisting of O, S, N, and NR wherein R is selected from the group consisting of hydrogen, C_{1-4} alkyl, and C_{1-4} acyl, said heterocycle being optionally substituted by C_{1-4} alkyl, C_{1-4} alkoxy, cyano, hydroxy, and amino, which may be unsubstituted or mono-or di-substituted by C_{1-4} alkyl, C_{1-4} acyl and trifluoroacyl; methoxy, cyano, C_{1-4} acetate, C_{1-4} acetyl and a group of the formula



wherein Y is selected from the group consisting of oxygen, sulfur, and CH_2:

R_9 and R_{10} are independently selected from the group consisting of hydrogen, fluorine, and iodine.

R_{11} is selected from the group consisting of hydroxyl, acetoxy, amino, dimethylamino, trifluoroacetamido, morpholino, cyano substituted morpholino, mono-, di-, tri-, or tetra-methoxy substituted morpholino, a group of the formula $NH(CH_2)_nCH(OR)_2$ wherein R is selected from the group consisting of C_{1-4} alkyl, C_{1-4} acyl or C_{7-8} aroyl and wherein n is 2 to 5, chloroalkylnitrosoureido of the formula $NH(CO)N(NO)(CH_2)_nCH_2Cl$ wherein n is 0 to 4, $NH(CH_2)_4CH(OAc)_2$, $NH(CH_2)_2OCH_2CH(OAc)_2$, and $NH(CO_2)OCH_2)CH_2CH(OAC)_2$:

R_{12} is selected from the group consisting of hydroxyl or its tetrahydropyranyl ether, benzoate, acetoxy, p-nitrobenzoate, amino, trifluoroacetamido, chloroethylnitrosoureido, fluorine, and

iodine;

R5 and R8 can also be independently selected from a 5 or 6 membered aromatic or non-aromatic heterocycle containing one or two heteroatoms selected from the group consisting of O, S, N, and NR wherein R is selected from the group consisting of hydrogen, C_{1-4} alkyl, and C_{1-4} acyl, said heterocycle being optionally substituted by C_{1-4} alkyl, C_{1-4} alkoxy, cyano, hydroxy, and amino, which may be unsubstituted or mono-or di-substituted by C_{1-4} alkyl, C_{1-4} acyl and trifluoroacyl.

A still further preferred compound of formula (12) are those wherein X_1 and X_2 are both oxygen;

X_3 is 0, S or SO;

X_4 is selected from the group consisting of N, or CQ;

R_1, R_2, R_3 and Q are each independently selected from the group consisting of hydrogen, fluorine, and hydroxyl, and methoxy.

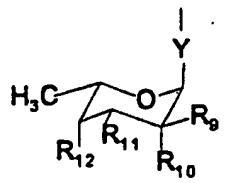
Z is one of C-R_6 or C-R_7.

R_6 is selected from the group consisting of C_{1-3} hydroxime, methyl, ethyl, C_{1-3} alkyl, hydroxymethyl, 1,2 dihydroxymethyl, a group of the formula -C(R)= X, wherein X is selected from the group of hydrogen and oxygen, and wherein R is selected from the group consisting of methyl, fluoromethyl, difluoromethyl, hydroxymethyl, acetoxymethyl, bromomethyl and C_{1-4} alkoxy, C_{2-3} alkenyl, C_{1-3} aceto, amino which may be unsubstituted or mono-or di-substituted by hydrogen, C_{1-3} alkyl, C_{2-3} acyl or a group of the formula -CHR*R** wherein R* and R** are independently selected from a hydrogen, C_{1-3} alkyl, a group of the formula -$(CH_2)_n$Z* wherein n is 0 to 2 and Z* is a C_{1-3} alkyl, and a group of the formula -NR*R** wherein R* and R** are independently selected from hydrogen, C_{1-3} alkyl and C_{1-3} acyl, Z* can also be a 5 or 6 membered aromatic or non-aromatic heterocycle containing one or two heteroatoms selected from the group consisting of O and N, said heterocycle being optionally substituted with a fluorine, a hydroxy, C_{1-3} alkoxy, and cyano; a 5 or 6 membered aromatic or non aromatic heterocycle containing one or two heteroatoms selected from the group consisting of O, S, N, and NH, said heterocycle being optionally substituted with one or more fluorine, hydroxy, methoxy, methyl, hydroxymethyl, cyano, amino and acylamino groups.

R_7 is selected from the group consisting of hydrogen, fluorine, methyl, and cyano;

R_5 and R_8 are independently selected from the group consisting of hydrogen, hydroxyl, bromine, chlorine, cyano, acetate, acetyl, and

a saccharide of the formula



wherein Y is selected from oxygen and CH_2, and

wherein R_9 and R_{10} are independently selected from the group consisting of hydrogen, fluorine, and iodine.

R_{11} is selected from the group consisting of amino, hydroxy, dimethylamino, acetoxy, trifluoroacetamido, morpholino, cyano substituted morpholino, methoxymorpholino and a group of the formula $NH(CH_2)_nCH(OR)_2$ wherein R is selected from a group consisting of methyl, acyl or benzoyl and wherein n is 3 to 5, chloroalkylnitrosoureido of the formula $NH(CO)N(NO)(CH_2)_nCH_2Cl$ wherein n is 0 to 4, and $NH(CH_2)OCH_2CH(OA_c)_2$

R_{12} is hydroxyl,iodine, or bromine.

Still further preferred compounds of formula (12) are those wherein

X_1 and X_2 are both oxygen.

X_3 is O or S.

X_4 is CQ.

R_2 and R_3 are both hydrogen.

R_1 and Q are independently selected from the group consisting of hydrogen, fluorine, and hydroxyl.

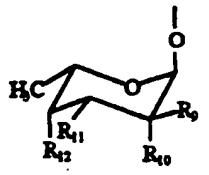
Z is one of C-R_6 or C-R_7.

R_6 is selected from the group consisting of ethyl, hydroxymethyl,

1,2-dihydroxyethyl, carbonyl, squarate, acyl of the formula -C(R)=0 wherein R is selected from the group consisting of methyl, fluoromethyl, difluoromethyl, hydroxymethyl.

R_7 is selected from the group consisting of hydrogen, methyl, or fluorine;

R_5 and R_8 are independently selected from the group consisting of hydrogen, hydroxyl, bromine, chlorine, cyano, acetate, acetyl and a saccharide of the formula

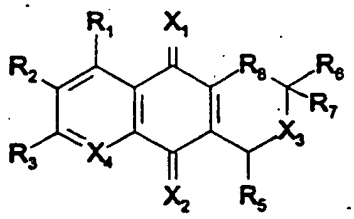


wherein R_9 and R_{10} are independently selected from the group consisting of hydrogen, fluorine, and iodine.

R_{11} is selected from the group consisting of hydroxyl, acetoxy, amino, dimethylamino, trifluoroacetamido, morpholino, cyano, substituted morpholino, methoxymorpholino;

R_{12} is selected from the group consisting of acetoxy, hydroxyl, hydrogen, and iodine, with the proviso that at least one of R_5 and R_8 is saccharide.

The invention also seeks to provide a process for the preparation of a compound of formula ,



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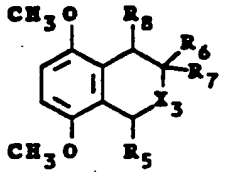
and pharmaceutically acceptable acid addition salts thereof wherein X_3 is selected from the group consisting NR, 0, or S, R_6 is methyl ketone or is as defined in claim 1; and R_1, R_2, R_3, R_5, R_6, R_7, R_8, X_1, X_2, X_4 and Z are as defined in claim 1

selected from the group of processes consisting of

I. 1) selecting a precursor isochroman compound of formula



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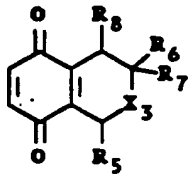
wherein R_5, R_6, R_7 and R_8 are defined as above, oxidatively demethylating said compound with an oxidant to give a quinone compound of formula



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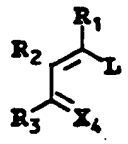
2) and cyclo-adding said quinone with a diene of formula



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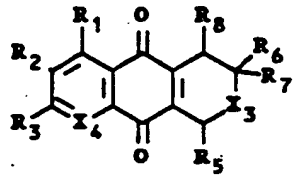
wherein L is a leaving group selected from the group consisting of halogen, tosyl, benzoyl, p-nitrobenzoyl and -OR or -SR, wherein R is selected from the group consisting of hydrogen, C_{1-16} alkyl, C_{1-16} acyl, C_{1-16} aryl, C_{3-16} alkylsilane, C_{8-16} alkylaryl silane and dimethylamino,

wherein R_1, R_2, R_3 and X_4 are as defined as above; to yield a tricyclic heteronaphthoquinone of formula



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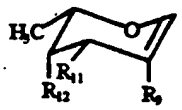
and

3) optionally coupling said tricyclic heteronaphthoquinone at R_5, wherein R_5 is -OH, to a saccharide of formula

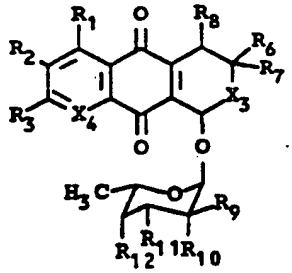
18a



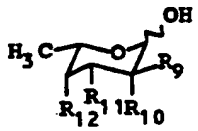
18b

wherein R_9, R_{10}, R_{11} and R_{12} are defined as in claim 1 and L is as defined above;

to yield a tricyclic saccharide of formula



II. a) coupling the isochroman (14) of reaction (I)(1), above, wherein R_5 is H, with a saccharide of formula



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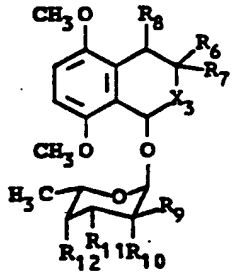
wherein R_9, R_{10}, R_{11} and R_{12} are as defined in claim 1 to yield a bicyclic saccharide of formula



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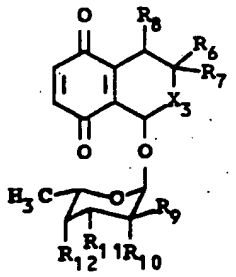
b) oxidatively demethylating the methoxy groups from formula (21) to yield a bicyclic quinone saccharide of formula



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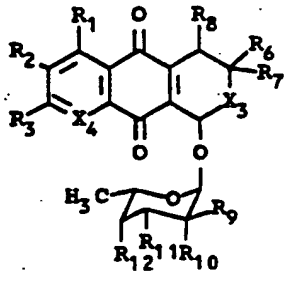
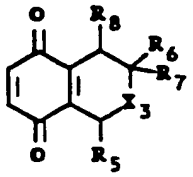
c) and cycloadding said chemical (19) with said diene (16) of reaction (I)(2) to yield the tricyclic saccharide

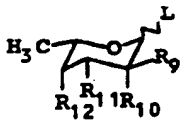


III. 1) coupling the quinone of formula 15,

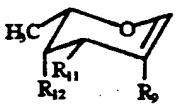


15

of step (I) (1), wherein R_5 is -OH, with a saccharide of the formula

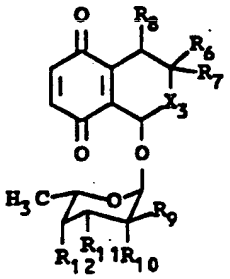


18a



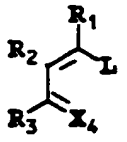
18b

of step (I) (2) to yield a bicyclic quinone sacharide of the formula

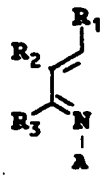


19

2) and cycloadding said quinone saccharide with the said diene of formula

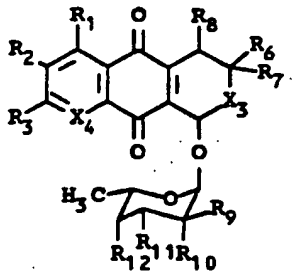


or

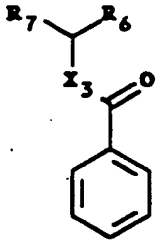


A is NR wherein R is selected from the group consisting of H, C_{1-16} alkyl, C_{7-16} acyl; and L is defined as above;

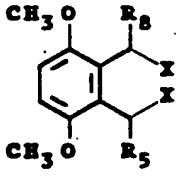
to yield a tricyclic saccharide of formula



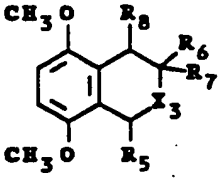
IV. a) selecting a precursor benzoate compound of formula



and condensing it with a dihalomethyl dimethoxybenzene wherein said halogens are independently selected from the group consisting of Cl, Br and I, and X_3 is selected from the group consisting of O, S, and N;



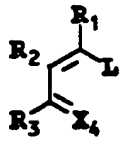
to yield a dimethoxyisochroman of formula,



14

b) oxidatively demethylating the methoxy groups from formula 14 to a bicyclic dioxoisochroman;

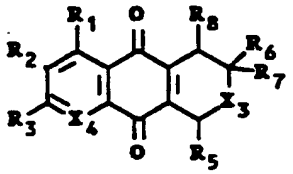
the resulting dioxoisochroman is cyclically coupled with the diene of formula



16

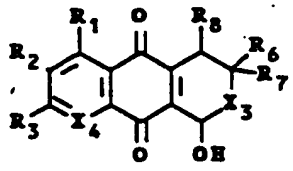
A is NR wherein R is selected from the group consisting of H, C_{1-16} alkyl, C_{7-16} aryl, and L is a leaving group as defined in (I)(2):

to yield an anthracenedione of formula



17

the resultant compound may optionally be converted to the hydroxyl form of formula

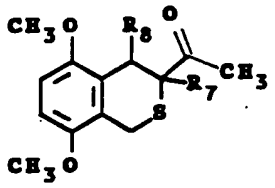


The quinones at positions X_1 and X_2 may be converted to other moities such as, for example, OH, S, NR, where R is hydrocarbon, and others. Such conversions are carried out using known methodology by chemists skilled in the art. For example, these conversions are taught in "The chemistry of the quinonoid Coumponds" V 1 and 2. John Wiley and Sons, 1988, which is incorporated by reference.

The compound may further be optionally coupled with a saccharide of formula 20 to yield the

tricyclic saccharide of formula 12;

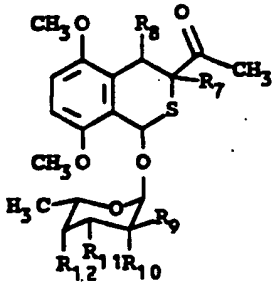
V. a dimethoxyisothiochroman of formula



may be optionally coupled with a saccharide of formula

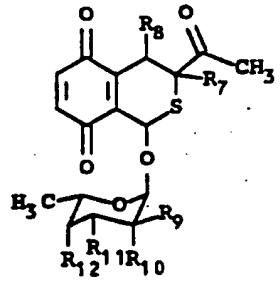
20

1) to yield a dimethoxybicyclic saccharide of formula



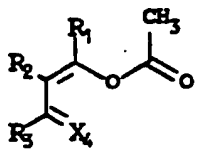
30

2) oxidatively demethylating the methoxy groups to yield a dioxobicyclic isochroman of formula



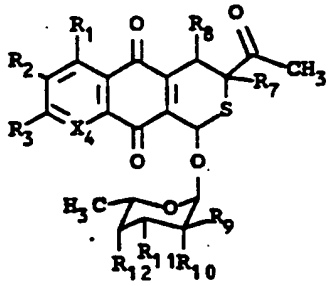
31

3) cycloadding said dioxobicyclic isothiochroman with a diene of formula 29

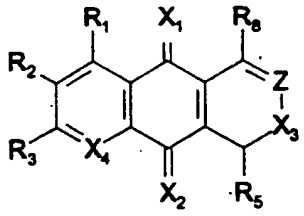


29

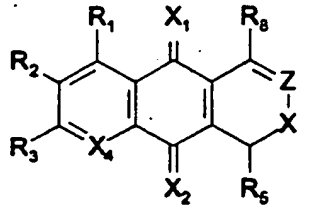
to yield a thiotricyclic saccharide of formula



Compounds of formula:



One obtained by treating a compound of formula:



with a base in the presence of air at an appropriate synthetic stage.

The term "alkyl" as employed herein includes both straight and branched chain radicals of up to 16 carbons, for example methyl, ethyl, propyl, isopropyl, butyl, t-butyl, isobutyl, pentyl, hexyl, isohexyl, heptyl, 4,4-dimethylpentyl, octyl, 2,2,4-trimethylpentyl, nonyl, decyl, undecyl, dodecyl, the various branched chain isomers thereof, as well as such groups including one or more halo substituent, such as F, Cl, Br, I or CF_3, one or more alkoxy sustituent, one or more hydroxy, a haloaryl substituent, one or more silyl group, one or more silyloxy group, a cycloalkyl substituent or an alkylcycloalkyl substituent.

The term "cycloalkyl" as used herein means a cycloalkyl group having 3 to 8 carbons, for example cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cyclopentylmethyl, cyclohexylmethyl, cyclohexylethyl, cycloheptyl and cyclooctyl.

The term "aryl" as employed herein refers to monocyclic or bicyclic aromatic groups containing from 6 to 10 carbons in the ring portion, such as phenyl, naphtyl, substituted phenyl, naphtyl, substituted phenyl or substituted naphthyl, wherein the substituent on either the phenyl or naphthyl may be for example C_{1-4} alkyl, halogen, C_{1-4} alkoxy, hydroxy or nitro.

The term "halogen" as used herein means chlorine, bromine, fluorine or iodine.

The term "aralkyl" as used herein refers to alkyl groups as discussed above having an aryl substituent, such as benzyl, p-nitrobenzyl, phenethyl, diphenylmethyl, and triphenylmethyl.

The term "aroyl" as used herein refers to a group of the formula -COAr wherein Ar denotes an "aryl" group as defined above.

The term "alkoxy" or "aralkoxy" as used herein includes any of the above alkyl or aralkyl groups linked to an oxygen atom.

The term "alkoxyalkyl" as used herein means any alkyl as discussed above linked to any alkoxy as discussed above, for example methoxymethyl.

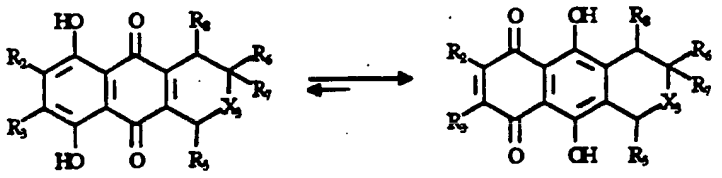
The term "aryloxyalkyl" as used herein means any alkyl as discussed above linked to an aryl as discussed above by an oxygen atom, for example phenoxymethyl.

The term "araloxyalkyl" as used herein means any aralkyl as discussed above linked to an alkyl as discussed above by an oxygen atom, for example benzyloxymethyl.

The term "acyloxyalkyl" as used herein means a C_{1-8} acyl group linked to an alkyl group as discussed above linked to an alkyl as discussed above by an oxygen atom, for example acetoxymethyl.

The term "hydroxyalkyl" as used herein means an alkyl group as discussed above bonded to a hydroxyl group as discussed above, for example, hydroxymethyl.

It will be appreciated by those skilled in the art that when R* = R_4 = hydroxyl and X_1=X_2=0 that compounds of formula (42) exist in equilibrium with tautomers of formula (43). Therefore, compounds of formula (43) are included within the scope of the invention.



42 43

(X_1=X_2 = O, R_1 = OH,X_4 = C-OH)

This invention also includes all the possible isomers and mixtures thereof, including diastereoisomeric mixtures and racemic mixtures, resulting from the possible combination of R or S stereochemical centers, when pertinent, at C_1, C_2 and C_3 as well as in all the other chiral centers.

This invention also comprises novel compounds which are prepared as intermediates or precursors of compounds of formulas (42) and (43). Such intermediate compounds are described hereinafter in connection with processes of preparing compounds of formulas (42) and (43).

Heteronaphthoquinones of general formula (12) are prepared by using Scheme I. With reference to Scheme I, new or known isochromans of formula 14, where R_5 is not a saccharide (PCT CA 9100208), are oxydatively demethylated with an oxidant such as ceric ammonium nitrate or silver oxide in an adequate solvent mixture such as acetonitrile-water, to give key isochromandiones of formula 15. Cycloaddition of this latter quinone with dienes of general formula 16 in a solvent such as toluene can give the tricyclic heteronaphthoquinone of formula 17. In the case when R_5 is a saccharide, two independent synthetic routes (A_2 or B) may be employed.

With respect to route A_2, glycosides of formula 12 (R_5 = Saccharide, X_1 = X_2 = O) are obtained by reacting appropriate aglycones of general structure 17, in which R_5 is an hydroxy, with known sugar derivatives of formula 18 in which R_9 to R^*_2 are as defined herein and L is a displaceable atom or group.

Suitable leaving groups, L, include halogen, for example iodine, bromine or chlorine, an unsubstituted or substituted benzoyl group such as p-nitrobenzoyl, and -OR or -SR, where R is an unsubstituted or substituted alkyl group, for example a C_{1-16} alkyl group such as methyl, ethyl or butyl, or R is an unsubstituted or substituted acyl group such as a C_{1-16} acyl group such as acetyl, or R is an unsubstituted or substituted aryl group or R is a C_3 to C_{10} trialkyl silyl such as trimethylsilyl or dimethyl-t-butylsilyl. Such sugars are obtained by derivatizing known saccharides of the family of

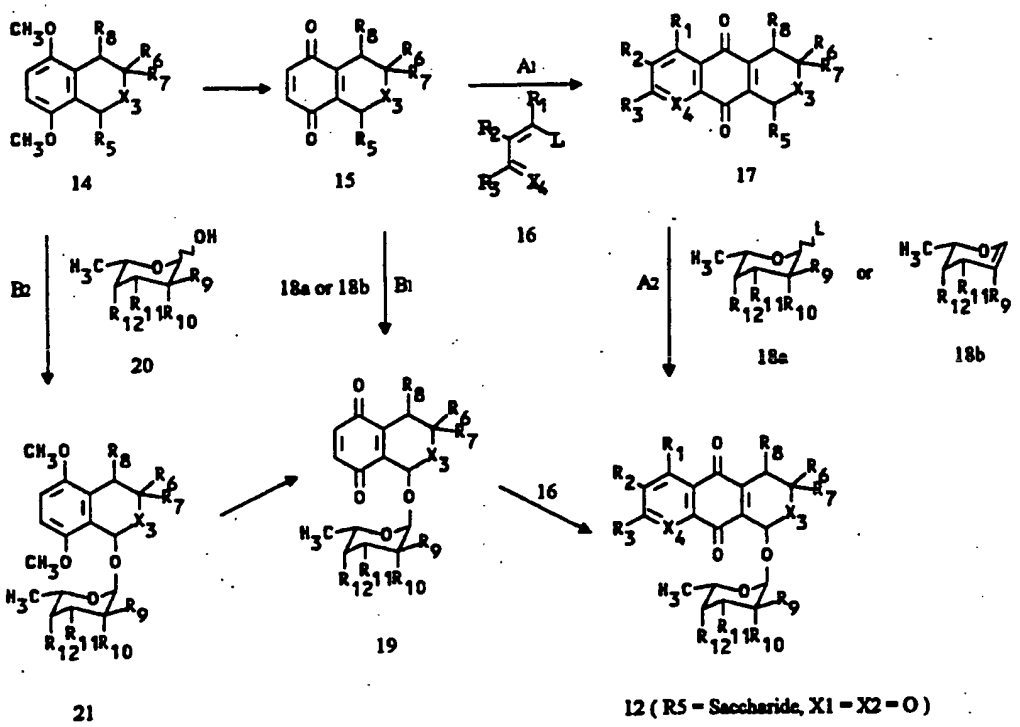
anthracycline antibiotics which are available from commercial or natural sources, (see for example, Monneret, C., Martini, A., Pais, M., Carbohydrate Research, 166, 59-70, 1987 and references therein; Acton, E.M., Tong, G.L., Mosher, C.W., and Wolgemuth, R.L., J. Med. Chem. 27, 638-645, 1984 and references therein; Arcamone F., Cancer Research, 45, 5995-5999, 1985 and references therein).

The aglycone of formula 17, is typically reacted with the appropriate sugar derivative of formula 18 in a compatible solvent such as methylene chloride using a Lewis acid such as titanium tetrachloride, stannic chloride, of trimethylsilyltrifluoromethane-sulfonate. Alternatively, as it is known in the art of anthracycline chemistry, when the leaving group of the sugar moiety is a halogen, the Koenigs-Knorr glycosidation or its modification may be used.

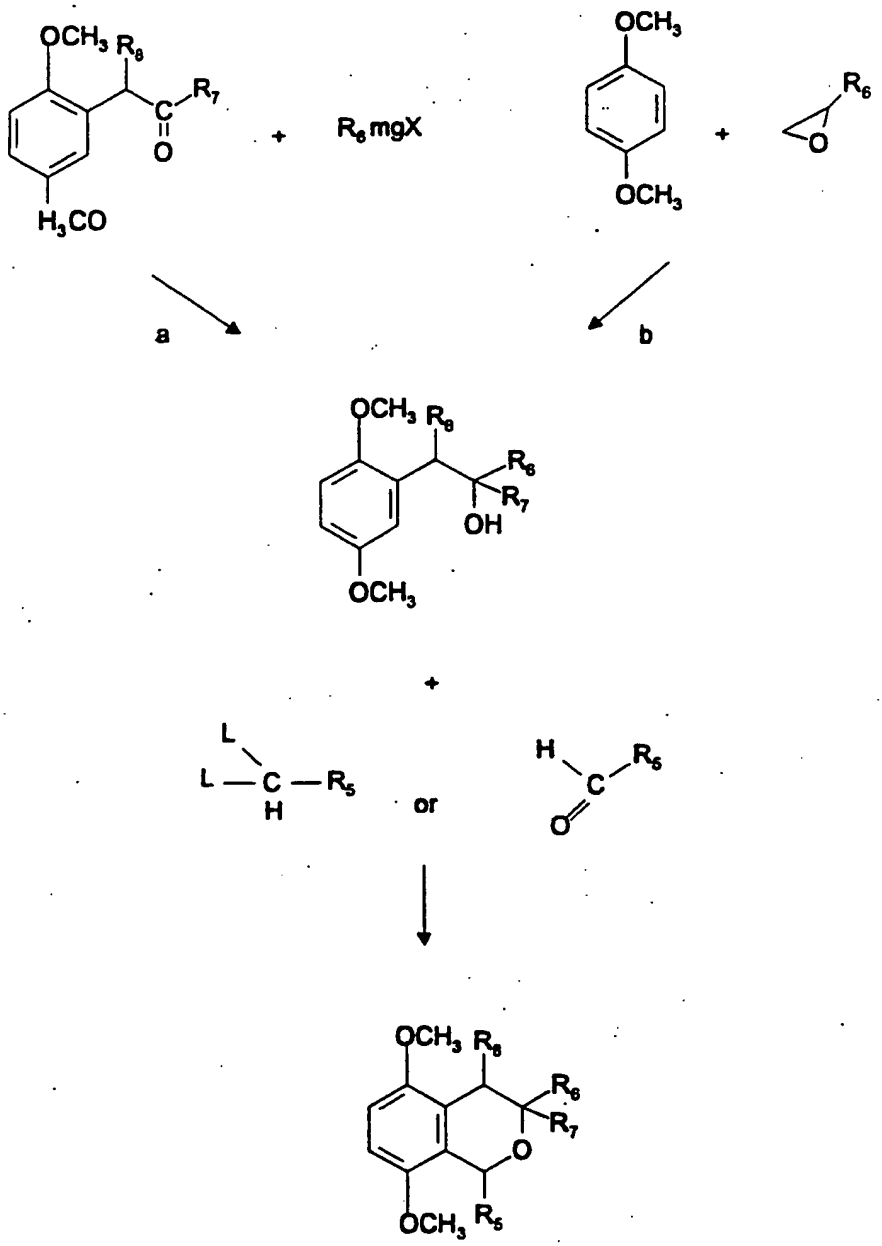
Alternatively glycosidation of 17 can be effected with known sugar derivates of formula 18b under protic catalysis to yield 12 (R_5 = Saccharide, $X_1 = X_2 = 0$).

In the event that the glycosidation of aglycone 17 is impractical then route B_1 or B_2 can be used to prepare glycosides of formula 12 (R_5 = saccharide, $X_1 = X_2 = 0$). With reference to route B_1, an isochromandione of formula 15, in which R_5 = OH, is glycosidated as described above for 17. Cycloaddition of intermediate 19 with dienes of formula 16 in a compatible solvent such as toluene or tetrahydrofuran yield the desired pyranonaphthoquinone glycosides of formula 12 (R_5 = saccharide, $X_1 = X_2 = 0$). Alternatively, glycosidated isochromandiones

Scheme I



Scheme 2



of formula 19 can be obtained via route B_2 by reacting isochromans of formula 14 with a saccharide of formula 20 in the presence of DDQ in a compatible solvent such as dichloromethane, and subsequent treatment of the glycosidated isochroman 21 with ceric ammonium nitrate using standard procedures.

It will also be appreciated that the following reactions may require the use of, or conveniently may be applied to, starting materials having protected functional groups, and deprotection might thus be required as an intermediate or final step to yield the desired compound. Protection and deprotection of functional groups may be effected using conventional means. Thus, for example, amino groups may be protected by a group selected from aralkyl (e.g. benzyl), acyl or aryl (e.g. 2,4-dinitrophenyl), subsequent removal of the protecting group being effected when desired by hydrolysis or hydrogenolysis as appropriate using standard conditions. Hydroxyl groups may be protected using any conventional hydroxyl protecting group, for example, as described in "Protective Groups in Organic Chemistry", Ed. J.F.W. McOmie (Plenum Press, 1973) or "Protective Groups in Organic Synthesis" by Theodora W. Greene (John Wiley and Sons, 1981, 1991). Examples of suitable hydroxyl protecting groups include groups selected from alkyl (e.g. methyl, t-butyl or methoxymethyl), aralkyl (e.g. benzyl, diphenylmethyl or triphenylmethyl), heterocyclic groups such as tetrahydropyranyl, acyl (e.g. acetyl or benzoyl), and silyl groups such as trialkylsilyl (e.g. t-butyldimethylsilyl). The hydroxyl protecting groups may be removed by conventional techniques. Thus, for example, alkyl, silyl, acyl and heterocyclic groups may be removed by solvolysis, e.g. by hydrolysis under acidic or basic conditions. Aralkyl groups such as triphenylmethyl may be similarly removed by solvolysis, e.g. by hydrolysis under acidic conditions. Aralkyl groups such as benzyl may be cleaved, for example, by treatment with BF_3/etherate and acetic anhydride followed by removal of acetate groups.

In the above processes, the compounds of formula (42) and (43) are generally obtained as a mixture of diastereoisomers. These isomers may be separated by conventional chromatography or fractional crystallization techniques.

Where the compound of formula (42) or (43) is desired as a single isomer, it may be obtained either by resolution of the final product or by stereospecific synthesis from isomerically pure starting material or any convenient intermediate.

Resolution of the final product, or an intermediate or starting material therefor, may be effected by any suitable method known in the art: see for example, "Stereochemistry of Carbon Compounds", by E.L. Eliel (McGraw Hill, 1962) and "Tables of Resolving Agents", by S.H. Wilen.

The compounds of the formula (12) and (13) possess anti-cancer and anti-tumor activity. While it is possible to administer one or more of the compounds of the invention as a raw chemical, it is preferred to administer the active ingredient(s) as a pharmaceutical composition.

In another aspect, the invention therefore provides pharmaceutical compositions primarily suitable for use as antitumor and anticancer agents, comprising an effective amount of at least one compound of the invention or a pharmaceutically acceptable derivative thereof in association with one or more pharmaceutically acceptable carriers and optionally other therapeutic and/or prophylactic ingredients. All the pharmaceutically acceptable salts for example the HCl and tartaric acid salts of the compounds useful as antitumor agents in mammals, including humans, are included in this invention.

It will be appreciated by those familiar with the art of clinical oncology that the compound(s) of this invention can be used in combination with other therapeutic agents, including chemotherapeutic agents (Cancer: Principles and Practices of Oncology, 3rd Edition, V.T. DeVito Jr., S. Hellman and S.A. Rosenberg; Antineoplastic Agents edited by W.A. Remers, John Wiley and Sons, N.Y., 1984). Thus, it will be understood that the compounds or pharmaceutical compositions of the invention may be formulated with the therapeutic agent to form a composition and administered to the patient or the compounds or compositions and the therapeutic agent may be administered separately, as appropriate for the medical condition being treated.

Therefore, for therapeutic purposes, a compound or composition of this invention can be used in association with one or more of the therapeutic agents belonging to any of the following groups:

1) Alkylating agents such as:
2-haloalkylamines (e.g. melphalan and chlorambucil);
2-haloalkylsulfides;
N-alkyl-N-nitrosoureas (e.g. carmustine, lomustine or semustine);
aryltriazines (e.g. decarbazine);
mitomycins (e.g. mitomycin C);
methylhydrazines (e.g. procarbazine);
bifunctional alkylating agents (e.g. mechlorethamine);
carbinolamines (e.g. sibiromycin);
streptozotocins and chlorozotocins;
phosphoramide mustards (e.g. cyclophosphamide);
urethane and hydantoin mustards

2) Antimetabolites such as:
mercaptopurines (e.g. 6-thioguanine and 6-[methylthio]purine);
azapyrimidines and pyrimidines;
hydroxyureas;
5-fluorouracil;
folic acid antagonists (e.g. amethopterin);
cytarabines;
prednisones;
diglycoaldehydes;
methotrexate;

3) Intercalators such as:
bleomycins and related glycoproteins;
anthracylines (e.g. doxorubicin, daunorubicin, epirubicin, esorubicin, idarubicin,

aclacinomycin A);

acridines (e.g. m-AMSA);

hycanthones;

ellipticines (e.g. 9-hydroxyellipticine);

actinomycins (e.g. actinocin);

anthraquinones (e.g. 1,4-bis[(aminoalkyl)-amino]-9,10-anthracenediones);

anthracene derivatives (e.g. pseudourea and bisanthrene);

phleomycins;

aureolic acids (e.g. mithramycin and olivomycin);

Camptothecins (e.g. topotecan);

4) Mitotic inhibitors such as:

dimeric catharanthus alkaloids (e.g. vincristine, vinblastine and vindesine);

colchicine derivatives (e.g. trimethylcolchicinic acid)

epipodophyllotoxins and podophylotoxins (e.g. etoposide and teniposide);

maytansinoids (e.g. maytansine and colubrinol);

terpenes (e.g. helenalin, tripdiolide and taxol);

steroids (e.g. 4ß-hyroxywithanolide E);

quassiniods (e.g. bruceantin);

pipobroman;

methylglyoxals (e.g. methylglyoxalbis-(thiosemicarbazone);

5) Hormones (e.g. estrogens, androgens, tamoxifen, nafoxidine, progesterone, glucocorticoids, mitotane, prolactin);

6) Immunostimulants (e.g. human interferons, levamisole and tilorane);

7) Monoclonal and polyclonal antibodies;

8) Radiosensitizing and radioprotecting compounds (e.g. metronidazole and misonidazole);

9) Other miscellaneous cytotoxic agents such as:

camptothecins;

quinolinequinones (e.g. streptonigrin and isopropylidene azastreptonigrin);

cisplatin, cisrhodium and related platinum series complexes;

tricothecenes (e.g. trichodermol or vermicarin A); cephalotoxines (e.g. harringtonine);

10)Cardioprotecting compounds, such as (±)-1,2-bis(3,5-dioxopiperazin-1-yl)

propane, commonly known as ICRF-187, and ICRF-198;

11) Drug-resistance reversal compounds such as P-glycoprotein inhibitors, for example Verapamil, cyclosporin-c, fujimycin;

12) Cytotoxic cells such as lymphokine activated killer -cells or T-cells,

13) Other Immunostimulants such as interleukin factors or antigens.

14) Polynucleotides of sence or antisensing nature.

15) Polynucleotides capable of forming triple helices with DNA or RNA.

16) Polyethers

17) Distamycin and analogs.

18) Taxanes such as taxol and taxotere.

The above list of possible therapeutic agents is not intended to limit this invention in any way.

The pharmaceutical compositions of the invention can be in forms suitable for oral, rectal, nasal, topical (including buccal and sublingual), vaginal or parenteral (including intraarterial, intraperitoneal, intramuscular, subcutaneous and intravenous administration), by inhalation or by insufflation. Where appropriate, the formulations may be conveniently presented in discrete dosage units and may be prepared by any method well known in the art of pharmacy. All methods include the step of bringing into association the active compound with liquid carriers or finely divided solid carriers or both and then, if necessary, shaping the product into the desired formulation.

For injectable use, the pharmaceutical composition forms include sterile aqueous solutions or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersions. In all cases, the form must be sterile and must be fluid to the extent that easy syringability exists. It must be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol for example, chremophor-EL, tween 80[1], glycerol, dimethyl sulfoxide (DMSO), propylene glycol, and liquid polyethylene glycol, and the like suitable mixtures thereof, and vegetable oils. The proper fluidity can be maintained for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of dispersion and by the use of surfactants. The prevention of the action of microorganisms can be brought about by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, sorbic acid, thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars or sodium chloride. Prolonged absorption of the injectable compositions can be brought about by the use in the compositions of agents delaying absorption, for example, aluminum monostearate and gelatin.

Sterile injectable solutions are prepared by incorporating the active ingredient or ingredients in the required amount in the appropriate solvent with various of the other ingredients enumerated above, as required, followed by filter sterilization. Generally, dispersions are prepared by incorporating the various sterilized active ingredients into a sterile vehicle which contains the basic dispersion medium and the

[1]denotes trademark

required other ingredients from those enumerated above. In the case of sterile powders for the preparation of sterile injectable solutions, the preferred methods of preparation are vacuum drying and the freeze-drying technique. These methods yield a powder of the active ingredient plus any additional desired ingredient from a previously sterile-filtered solution thereof.

Pharmaceutical formulations suitable for oral administration may conveniently be presented as discrete units such as capsules, sachets or tablets each containing a predetermined amount of the active ingredient; as a powder or granules; as a solution; as a suspension; or as an emulsion. The active ingredient may also be presented as a bolus, electuary or paste. Tablets and capsules for oral administration may contain conventional excipients such as binding agents, fillers, lubricants, disintegrants, or wetting agents. The tablets may be coated according to methods well known in the art. Oral liquid preparations may be in the form of, for example, aqueous or oily suspensions, solutions, emulsions, syrups or elixirs, or may be presented as a dry product for constitution with water or other suitable vehicle before use. Such liquid preparations may contain conventional additives such as suspending agents, emulsifying agents, non-aqueous vehicles (which may include edible oils) or preservatives.

As used herein, the expression "pharmaceutically acceptable carrier" includes any and all solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic and absorption delaying agents and the like. The use of such media and agents for pharmaceutically active substances is well known in the art. Except isofar as any conventional media or agent is incompatible with the active ingredient, its use in the present compositions is contemplated. Supplementary active ingredients can be incorporated into the inventive compositions.

It is especially advantageous to formulate compositions in dosage unit form for ease of administration and uniformity of dosage. Dosage unit form as used in the specification and claims herein refers to physically discrete units suited as unitary dosages for the animal subjects to be treated, each unit containing a predetermined quantity of active material calculated to produce the desired therapeutic effect in association with the required pharmaceutical carrier. The specification for the novel dosage unit forms of the invention are dictated by and directly dependent on (a) the unique characteristics of the active material and the particular therapeutic effect to be achieved and (b) the limitations inherent in the art of compounding such an active material for the treatment of disease in living subjects having a diseased condition in which bodily health is impaired as disclosed in detail in this specification.

The dosage of the principal active ingredient for the treatment of the indicated conditions depends upon the age, weight and condition of the subject being treated; the particular condition and its severity; the particular form of the active ingredient, the potency of the active ingredient, and the route of administration. A daily dose of from about 0.001 to about 100 mg/kg of body weight given singly or in divided doses of up to 5 times a day or by continuous infusion embraces the effective range for the treatment of most conditions for which the novel compounds are effective. For a 75 kg subject, this translates into between about .075 and about 7500 mg/day. If the dosage is divided for example, into three individual dosages, these will range from about .25 to about 2500 mg. of the active ingredient. The preferred range is from about 0.1 to about 50 mg/kg of body weight/day with about 0.2 to about 30

mg/kg of body weight/day being more preferred.

The principal active ingredient is compounded for convenient and effective administration in effective amounts with a suitable pharmaceutically acceptable carrier in dosage unit form as hereinbefore disclosed. A unit dosage form can, for example, contain the principal active ingredient in amounts ranging from about 0.1 to about 1000 mg., with from about 1.0 to about 500 mg. being preferred. Expressed in proportions, the active ingredient is generally present in from about 0.1 to about 500 mg/ml of carrier. In the case of compositions containing supplementary active ingredients, the dosages are determined by reference to the usual dose and manner of administration of the said ingredients.

Antitumor treatment comprises the administration of any of the compounds of this invention in an acceptable pharmaceutical formulation at the effective therapeutic dosage. It is understood that chemotherapy can require the use of any of the compounds of this invention bound to an agent which facilitates targeting the compound to the tumor cells. The agent may be chosen from, for example, monoclonal or polyclonal antibodies, proteins and liposomes. The compounds of this invention could also be administered as monomeric, dimeric, trimeric or oligomeric metal chelate complexes with, for example iron, magnesium or calcium.

The compounds of the invention exhibit antitumor activity, most notably, antitumor activity with human breast cancer, leukemia, colon cancer, ovarian cancer, and melanoma. This list of conditions is however not exclusive, and it is believed that the compounds of the invention will exhibit activity against other tumors and cancers, such as for example pancreatic cancer, bladder cancer, lung cancer, and central nervous system (CNS) cancer. Most notably the compounds of this invention are more potent than doxorubicin against P-170 mediated multidrug resistant cancers.

EXAMPLE 1

Methyl (5,10-dioxo-3,4,5,10-tetrahydronaphtho [2,3- C] pyran-3-yl) ketone BCH-1125

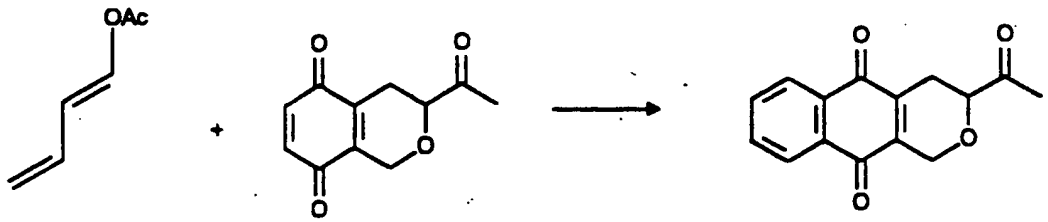
A mixture of methyl (5,8-dioxo-3,4,5,8-tetrahydrobenzo [2,3-C] pyran-3-yl) ketone (100 mg, 0.485 mmol) and acetoxybutadiene (75 µl, 0.630 mmol) in dry benzene (5 mL) was heated for 12 hours at 60°C under argon atmosphere. The solvent was then removed in vacuo and the resulting adduct dried under reduced pressure. The adduct was dissolved in 10 mL of ethanol and to this solution was added 1 mL of 1% K_2CO_3 aqueous solution. After stirring for 2 hours at R.T., the reaction mixture was neutralized (pH=6) and extracted with CH_2Cl_2 (2x50 mL). The organic layer was then washed with water (3x50 mL) and dried over $MgSO_4$. Flash chromatography (toluene: ethyl acetate; 95%:5%) of the residue gave 69 mg (55% yield) of pure titled compound. (MP: 135-136°C).

PMR ($CDCl_3$,250MHz): 2.31 (s,3H,CH_3), 2.54 (dddd,1H,J=18.0, 10.3,3.6 and 1.8Hz,HCHa-CH), 2.97 (dm,1H,J=19 and 3.0Hz,HCHe-CH=), 4.05 (dd, 1H,J=10.3 and 3.9Hz, CH_2-CH), 4.58 (dt,1H,J=18.7 and 3.6Hz,HCHa-O), 4.92 (dd,1H,J=18.7 and 1.8Hz,HCHe-O), 7.72 (m,2H,Ar-H), 8.04 (m,2H,Ar-H).

CMR _($CDCl_3$,75.44 MHz): 24.42 (CH_2-CH), 26,57 (COCH_3), 63.97(CH_2-O-), 78.63 (CH_2-CH), 126.70, 127.08, 132.36 and 134.52 (CH aromatic); 132.20, 134.42, 141.30, and 142.41 (C quaternary),

183.51 and 183.63 (C=O quinone), 207.25 (CO-CH_3).

EXAMPLE 1



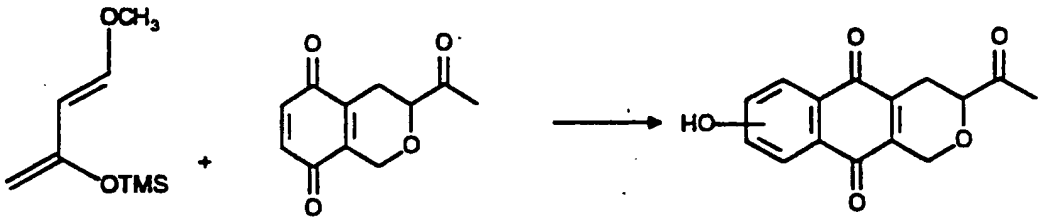
EXAMPLE 2

Methyl (7-hydroxy-5,10-dioxo-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone BCH-1129

A mixture of 1-methoxy-3-trimethylsilyloxy butadiene (776 mg, 4.51 mmol) and methyl (5,8-dioxo-3,4,5,8-tetrahydrobenzo [2,3-C] pyran-3-yl) ketone (309 mg, 1.50 mmol) in 6mL of dry toluene was stirred for 90 minutes at room temperature under argon atmosphere. The solvent was then removed in vacuo and the dried residue was dissolved in 10 mL of THF. To this solution was added 2 mL of a 4% aq. HCl solution. The combined organic layers were then washed with water and dried over $MgSO_4$. Flash chromatography (toluene: ethyl acetate; 95%:5%) of the residue gave 180 mg (65% yield) of the titled compound (MP: 169-170°C).

PMR (DMSO-d_6, 250 MHz): 2.24 (s,3H,CH_3), 2.45 (m,1H,HCHa-CH=), 2.77 (dd,1H,J=19 and 3.0Hz,HCHe-CH),4.20 (dd,1H,J=9.8 and 3.9Hz,CH_2-CH), 4.55 (d overlapped, 1H, J=22 Hz,HCHa-O-), 4.78 (d overlapped, 1H, J= 18.0Hz,HCHe-O), 7.15 (dd,1H,J=8.5 and 2.4Hz,Ar-H), 7.30 (2d, 1H, J=2.5Hz,Ar-H), 7.88 (2d,1H,J=9.1Hz,Ar-H), 10.96 (s,1H,Ar-OH).

EXAMPLE 2



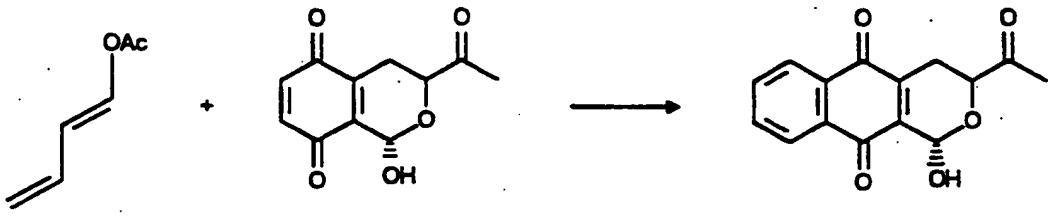
EXAMPLE 3

Methyl (1-hydroxy-5,10-dioxo-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone BCH-1148

A mixture of methyl (1-methoxy-5,8 dioxo-tetrahydrobenzo [2,3-C] pyran-3-yl) ketone (100 mg, 0.450 mmol) and acetoxy butadiene (80 μg, 0.675 mmol) in dry benzene (5 mL) was heated for 3 hours at 60°C under argon atmosphere. The solvent was then removed *in vacuo* and the resultting adduct was dissolved in 10 mL of toluene and then aromatized on silica gel by flash chromatography (toluene: ethyl acetate; 90%:10% followed by 70%:30%). Evaporation of the solvents gave 37 mg (31% yield) of pure titled compound.

PMR (Acetone d_6, 250 MHz): 2.26 (s,3H,$COCH_3$), 2,50 (dd,1H,J=11.6, 19.5Hz,HCHa-CH), 2.89 (dd,1H,J=4.2,19.5Hz,HCHe-CH), 4.71 (dd,1H, J=4.2,11.6 Hz,CH-CH_2); 6.12 (broad s,1H,CHOH); 7.87 (m,2H,ArH); 8.07 (m,2H, ArH).

EXAMPLE 3



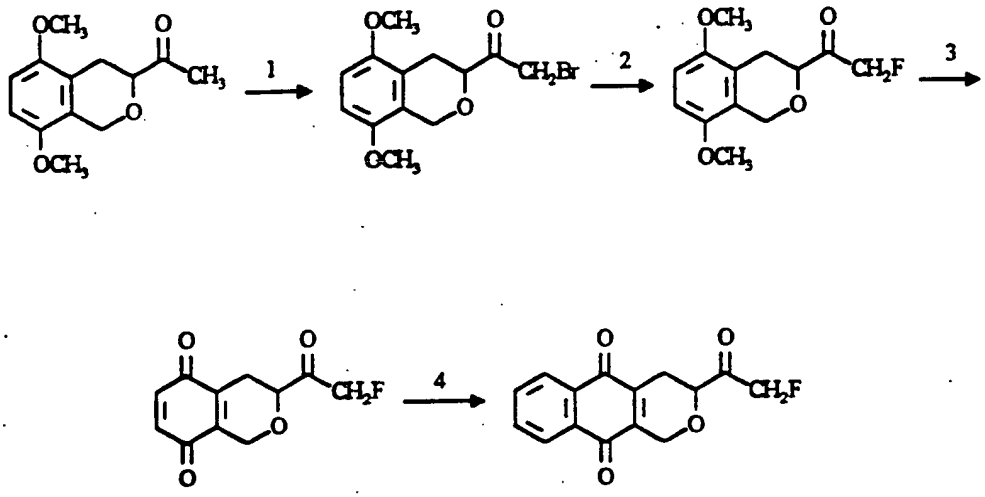
EXAMPLE 4 - Monofluoromethyl (5,10-dioxo-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone

Step 1: Monobromomethyl (5,8-dimethoxy-3,4-dihydrobenzo [2,3-C] pyran-3-yl) ketone

To a stirred solution of methyl (5,8-dimethoxy-3,4-dihydrobenzo [2,3-c] pyran-3-yl) ketone (1.905g, 8.04 mmol) and trimethylsilyl chloride (1,530 μl, 12.0 mmol) in tetrahydrofuran (48ml) under nitrogen, at -78°C, was slowly added lithium diisopropyl amide (diisopropyl amine 10.71 mmol, n-butyl lithium 4.26 ml of a 2.5M solution in tetrahydrofuran, and 6.0 ml of tetrahydrofuran). After stirring for 10 minutes the temperature was raised to 0°C, and stirring was continued for 10 more minutes. Solvent was removed and the crude product was dissolved in 48 ml of tetrahydrofuran, N-bromosuccinamide (1,716 mg, 9.66 mmol) was added slowly to the solution. After 10 minutes, the reaction system was worked up with saturated aqueous sodium bicarbonate and washed with brine. The titled compound was obtained following flash chromatography (hexanes:ethyl acetate, 9:1) of the crude product. ^1H NMR (benzene-d_6, 250 MHz) _: 2.68 (dd, 1H,HCHa), 3.16 (dd,1H,HCHe), 3.28 (s,3H,OCH_3), 3.32 (s,3H,OCH_3), 3.73

(dd,1H,J=4.0,11.5Hz,CH), 3.81 (dd,2H,CH_2Br), 4.51 (d,1H, J=15.8Hz, HCHaO), 5.05 (d,1H,J=15.8Hz,HCHeO), 6.335 (dd,2H,ArH).

Example 4: Monofluoromethyl (5,10-dioxo-3,4,5,10-tetrahydronaphto[2,3-C] pyran-3-yl) ketone.



Step 2: Monofluoromethyl (5,8-dimethoxy-3,4-dihydrobenzo [2,3-C]-pyran-3-yl) ketone

To a solution of 1 equivalent (3.75 mM, 1.18 g) of bromomethyl ketone isochroman from step 1 and 3 equivalents (11.25 mM, 2.160 g) of pTSA in 20 mL of dry THF was added slowly, at R.T., 6 equi. (22.5 mM, 22.5 mL) of a 1M solution in THF of $N^+(Bu)_4F^-$. After stirring one night at R.T., 15 mL of H_2O were added and the mixture was extracted with 3x20 mL of ethyl acetate. After drying with $NaSO_4$ and solvent evaporation, the residue was flash chromatographed (Toluene: Ethyl acetate; 9.5:0.5) to give a 50% yield of pure titled compound.

^1H NMR (250 MHz, $CDCl_3$): 2.61 (dd,1H,HCHa), 3.11 (dd,1H,HCHe), 4.27 (dd,1H,CH), 4.63 (d,1H,HCHaO), 4.99 (d,1H,HCHeO), 5.33 (d, 2H, CH_2F), 6.67 (dd,2H,ArH).

Step 3. Monofluoromethyl (5,8-dioxo-3,4,5,8-tetrahydrobenzo [2,3-C] pyran-3-yl) ketone

To 1 equivalent (0.220 mM, 56 mg) of the fluoromethylketone isochroman from step 2 dissolved in 3 mL of acetonitrile at 0°C was added 3 equivalents of ceric ammonium nitrate (0.66 mM). After 10 minutes, the reaction mixture was brought to R.T., stirred for 20 minutes, and then extracted with dichloromethane/THF (1/1). The organic layer was dried over $MgSO_4$. The titled quinone was obtained (67 mg) following evaporation of solvent.

^1H NMR (250 MHz, $CDCl_3$): ^1H NMR (250 MHz, $CDCl_3$) _: 2.46

(dddd,1H,J=3.0,4.0,10.4,18.9Hz,HCHa), 2.91 (dt, 1H, J=3.5, 18.9Hz, HCHe), 4.25 (dd,J=3.8,10.4Hz,CH), 4.445 (dt,J=3.5,18.4Hz,HCHaO), 4.77 (dd,J=2.2,18.5Hz,HCHeO), 5.25 (d,2H,CH_2F), 6.75 (dd,2H,HC=CH).

Step 4. Monofluoromethyl (5,10-dioxo-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone

To 1 equivalent (0.220 mM, 50 mg) of the fluoroquinone from step 3 dissolved in 5 mL of dry toluene was added 1.3 equivalents (0.286 mM, 32.0 mg, 35 µl) of acetoxy butadiene and stirred overnight. The reaction mixture was passed directly on a silica gel column. 20 mg of pure titled compound was isolated after two flash chromatography (2% EtOAc in toluene).

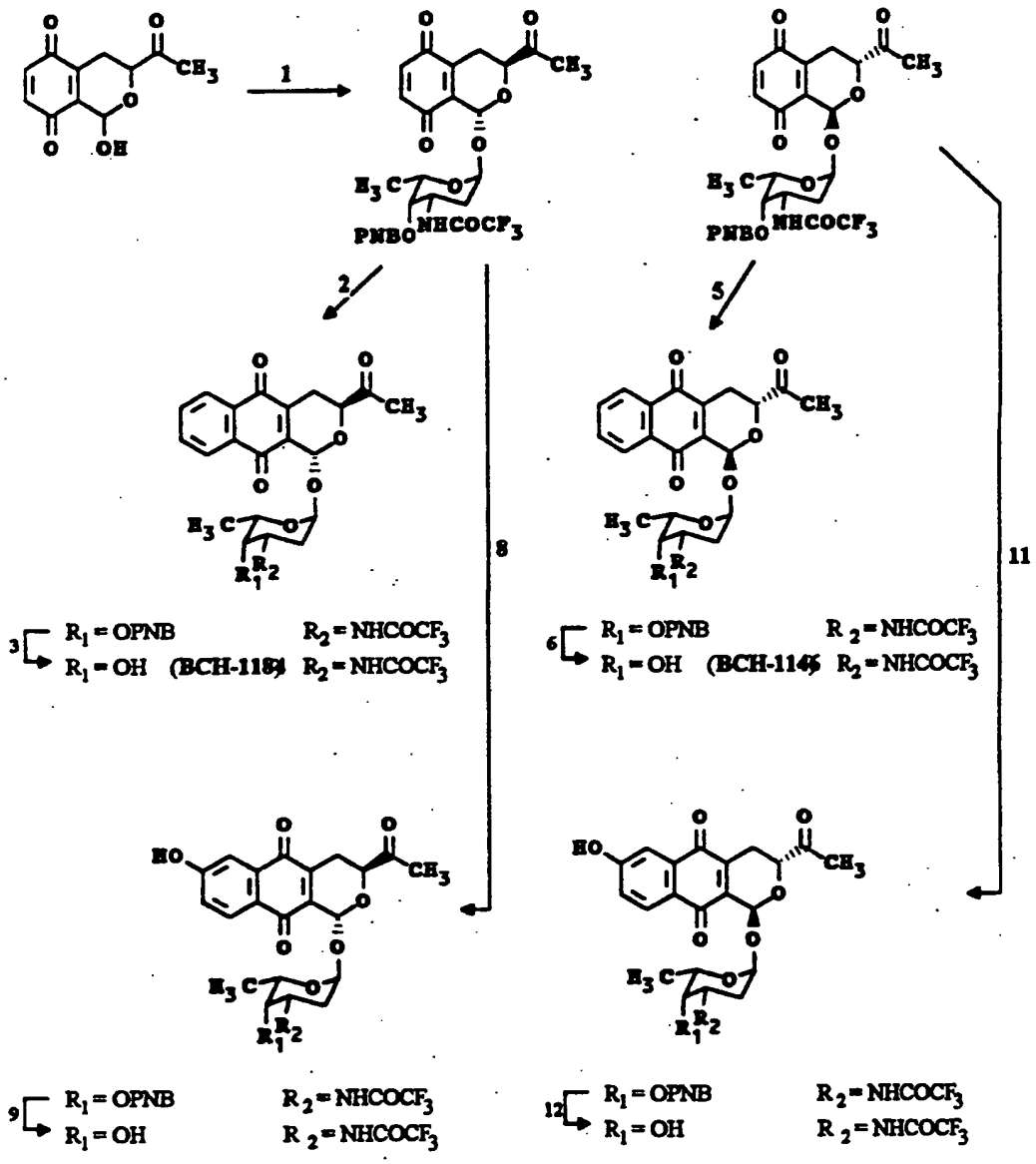
PMR (Acetone-d_6, 250 MHz): 2.62 (dddd,1H,HCHa), 2.94 (dt,1H,HCHe), 4.46 (dd,1H,CH), 4.62 (dt,1H,HCHa), 4.84 (dd,1H,HCHe), 5.43 (d, 2H, CH_2F), 7.83 (m,2H,ArH), 8.03 (m,2H,ArH).

EXAMPLE 5

Step 1.
(1'S,1R,3S) and (1'S,1S,3R)-Methyl (5,8-dioxo-1-(2',3', 6'- trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-3,4,5,8-tetrahydrobenzo [2,3-C] pyran-3-yl) ketone

To a stirred solution of 1,4-di-O-p-nitrobenzoyl-N-trifluoroacyl daunosamine (1.584 g, 2.93 mmol) in 160 mL of dry dichloromethane and 40 mL of anhydrous ether, maintained at -35°C under argon atmosphere, was added dropwise 1.132 mL (5.85 mmol) of trimethyl silyl triflate (TMSOTf). After stirring for 1.5 hours at 0°C, the temperature was lowered to -15°C and a cooled (0°C) solution of methyl (1-hydroxy-5,8-dioxo-3,4,5,8-tetrahydrobenzo [2,3-C] pyran-3-yl) ketone in dry dichloromethane (40 mL) was added. After 5 hours of stirring, the reaction mixture was put into a solution of 150 mL of ethyl acetate and 50 mL of a saturated $NaHCO_3$ solution. The organic layer was washed with water and dried (Na_2SO_4). Flash chromatography of the residue gave 917 mg (69% yield) of the mixture of titled stereoisomers.

Example 5: Glycosidated derivatives of pyranonaphtoquinones with a methyl ketone side chain.



A second flash chromatography seperated the individual diastereomers.

The 1'S,1S,3R titled diastereomer had ^{1}H NMR (250 MHz, acetone-d_6) _: 1.28 (d,3H,J=6.4Hz,CH_3), 2.05 (hidden m, 1H,2'-CH_2), 2.30 (s,1H, $COCH_3$), 2.42-2.49 (m,2H,2'-CH_2 overlapped with HCHa), 2.84 (dd,1H,HCHe,) 4.53-4.65 (broad m,1H,3'-CH), 4.635 (dd,2H,J=4.2, 11.6Hz,O-CH-$COCH_3$), 4.76 (broad q,1H,5'-CH), 5.50 (broad s,1H,4'-CH), 5.69 (broad s,1H,1'-CH), 6.02 (s,1H,O-CH-O), 6.90 (dd,2H,2X C= CH), 8.37 (m,4H,ArH), 8.68 (broad d,1H,NH).

The 1'S,1R,3S titled diastereomer had ^{1}H NMR (250 MHz, acetone-d_6) _: 1.19 (d,3H,J=6.6Hz,CH_3), 1.89 (dd,1H,J=4.6,13.1Hz,2'-CH_2),2.32 (s, 3H,$COCH_3$), 2.29-2.47 (m,2H,2'-CH_2 overlapped with HCHa), 2.89 (dd,1H, J=4.1Hz,HCHe), 4.60 (m,2H,3'-CH overlapped with 5'-CH), 4.71 (dd,1H, J=4.1,11.5Hz,O-CH-$COCH_3$), 5.48 (broad s, 1H,4'-CH), 5.64 (broad s, 1H,1'-CH), 5.89 (s,1H,O-CH-O), 6.87 (dd,2H,2XC=CH), 8.37 (dd,4H, ArH), 8.69 (broad d, 1H, NH).

Step 2.

(1'S,1R,3S)-Methyl (5,10-dioxo-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexo-pyranose)-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone

To a stirred solution of 1'S, 1R, 1S -diastereomer, from step 1 (Example 5), (0.464 mmol) in dry benzene (10 mL) under argon was added 78μl (696 mL) of 1-acetoxybutadiene. After stirring for 16 hours at room temperature, the reaction mixture was flash chromatographed (toluene:ethyl acetate; 90%:10%) to give 244 mg (82% yield) of the pure titled compound.

^{1}H NMR (250 MHz, acetone-d_6): 1.22 (d,3H,J=6.4Hz,CH_3), 1.94 (dd,1H,J=4.7,13.1Hz,2'-CH_2), 2.35 (s,3H,$COCH_3$), 2.42 (m,1H,2'-CH_2), 2.52 (dd,1H,J=11.6,19.8Hz,HCHa), 3.04 (dd,1H,J=3.9,19.6 Hz, HCHe), 4.55-4.68 (overlapped m,2H,3'-CH and 5'-CH), 4.79 (dd,1H,J=4.0,11.5 Hz,O-CH-$COCH_3$), 5.49 (broad s,1H,4'-CH), 5.75 (broad s,1H,1'-CH), 6.07 (s,1H,O-CH-O), 7.83-7.93 (m,2H,ArH), 8.06-8.14 (m,2H,ArH), 8.32-8.43 (m,4H,ArH), 8.67 (broad d,1H,NH).

Step 3.

(1'S,1R,3S)-Methyl (5,10-dioxo-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-hydroxy-L-lyxohexopyranose)-3,4,5, 10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone BCH-1184

To a stirred solution of the glycoside from step 2, (30 mg, 4.65×10^{-5} mmol) in 4 mL of dry methanol and 1 mL of anhydrous THF at 0°C and under argon, was added 11μl (4.66×10^{-5} mmol) of $NaOCH_3$ (4.37 M) solution in methanol. After 5 minutes of stirring, the reaction was quenched with 1 mL of saturated NH_4Cl solution and extracted with CH_2Cl_2 . Following evaporation of solvent, flash chromatography of the residue gave 23 mg (100% yield) of pure titled compound.

^{1}H NMR (250 MHz, Acetone-d_6): 1.25 (d,3H,J=6.5Hz,CH_3), 1.76 (dd,1H, J=4.5,12.9Hz,2'-CH_2), 2.16 (m,1H,2'-CH_2), 2.32 (s,3H,$COCH_3$), 2.48(dd, J=11.6,19.5Hz,HCHa), 2.99 (dd,1H,J=4.1,19.5 Hz,HCHe), 3.68 (broad s,1H,4'-CH), 4.17-4.41 (overlapped m,2H,3'-CH and 5'-CH), 4.69 (dd, 1H,J=4.0,11.0Hz,O-CH-$COCH_3$), 5.53 (broad s,1H,1'-CH), 5.97 (s,1H,O-CH-O), 7.82-7.90 (m,2H,ArH), 8.01-8.05 (m,2H,ArH), 8.13 (broad d, 1H,NH).

Step 4:

(1'S,1S,3R)-Methyl (5,10-dioxo-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexo-pyranose)-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone

Application of the procedure described in step 2 of the present example on the 1'S, 1S, 3R quinone glycoside from step 1 gave the titled compound which had:

^{1}H NMR (250 MHz, Acetone-d_6): 1.33 (d,3H,J=6.6Hz,CH_3),1.94 to 2.08 (m,1H,2'-CH_2), 2.33 (s,3H,$COCH_3$), 2.49 (m,1H,2'-CH_2), 2.58 (dd,1H, J=11.7,19.6Hz,HCHa), 3.01 (dd,1H,J=4.1,19.7Hz,HCHe), 4.53-4.65 (m, 1H,3'-CH), 4.71 (dd,1H,J=4.1,11.5 Hz,O-CH-$COCH_3$), 4.90 (broad q,1H, 5'-CH), 5.53 (broad s,1H,4'-CH), 5.75 (broad s,1H,1'-CH), 6.21 (s, 1H,O-CH-O), 7.88-7.92 (m,2H,ArH), 8.08-8.16 (m,2H,ArH), 8.34-8.43 (m,4H,ArH), 8.69 (broad d,1H,NH).

Step 5:

(1'S,1S,3R)-Methyl (5,10-dioxo-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-hydroxy-L-lyxohexopyranose)-3,4,5, 10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone BCH-1146

Treatment of the glycoside obtained from step 5 with sodium methoxide as described in step 3 of this example yielded the titled compound, which had:

^{1}H NMR (250 MHz, Acetone-d_6) 1.35 (d,3H,J=6.4Hz,CH_3), 1.77(dd,1H, J=4.5,12.9Hz,2'-CH_2), 2.17 (dt,1H,J= 3.7,12.9Hz,2'-CH_2), 2.30 (s,3H, $COCH_3$), 2.56 (dd,1H,J=10.7,19.6Hz,HCHa), 2.98 (dd,1H,J=4.2,19.8 Hz, HCHe),3.70 (broad s,1H,4'-CH), 4.2-4.4 (m,1H,3'- CH), 4.60 (broad quartet,1H,5'-CH), 4.66 (dd,1H,J=4.2,11.5Hz,O-CH-$COCH_3$), 5.52 (broad d,1H,1'-CH), 6.15 (s,1H,O-CH-O), 7.86-7.92 (m,2H,ArH), 8.07-8.11 (m,2H,ArH), 8.15 (broad d,1H,NH).

Step 6:

(1'S,1R,3S)-Methyl (5,10-dioxo-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexo-pyranose)-7-hydroxy-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone

The titled compound was prepared in 62% yield by cyclocondensing the 1'S, 1R, 3S-quinone glycoside from step 1 of this example with 1-methoxy-3-trimethylsilyloxybutadiene. The same procedure as described in step 2, in this example, was used.

^{1}H NMR (250 MHz, Acetone-d_6): 1.21 (d,3H,J=6.6Hz,CH_3), 1.93 (m,1H, 2'-CH_2), 2.34 (s,3H,$COCH_3$), 2.49 (dd,1H,J=11.6,19.5Hz,HCHa), 3.00 (dd,1H,J=4.1,19.5Hz,HCHe), 4.57-4.69 (overlapped multiplets, 2H,3'-CH and 5'-CH),4.76 (dd,1H,J=4.0,11.5Hz,0-CH-$COCH_3$), 5.49 (broad s, 1H,4'-CH), 5.73 (broad d,1H,1'-CH), 6.04 (s,1H,O-CH-O), 7.25 (dd, 1H,J=2.5,8.5Hz,ArH), 7.46 (d,1H,J=2.5Hz,ArH), 7.98 (d,1H,J= 8.6Hz, ArH), 8.38 (m,4H,ArH), 8.58 (broad d,1H,NH) 10.23

(broad s,1H, ArOH).

Step 7:

(1'S,1R,3S)-Methyl (5,10-dioxo-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-7-hydroxy-3,4,5, 10-tetrahydro [2,3-C] pyran-3-yl) ketone BCH-1181

Application of the hydrolysis procedure described in step 3 of this example to the 1'S, 1R, 3S tricyclic glycoside of step 8 resulted in the removal of the p-nitrobenzoyl protecting group. The titled compound had:

^{1}H NMR (250 MHz, Acetone-d_6): 1.63 (d,3H,J=6.4Hz,CH_3), 2.14 (m,1H, 2'-CH_2), 2.53 (m,1H,2'-CH_2), 2.70 (s,3H,$COCH_3$), 2.87 (dd,1H,J=11.7, 19.4Hz,HCHa), 3.35 (dd,1H,J=4.1,19.4Hz,HCHe), 4.07 (broad s,1H,4'-CH), 4.65 (overlapped m,2H,3'-CH and 5'-CH), 5.07 (dd,1H,J=4.1,11.7 Hz,0-CH-$COCH_3$), 5.91 (broad d,1H,1'-CH), 6.35 (s,1H,O-CH-O), 7.64 (dd,1H,J=2.5,8.5Hz,ArH), 7.84 (d,1H,J=2.5Hz,ArH), 8.35 (d,1H,J= 8.5 Hz,ArH), 8.48 (broad d,1H,NH), 10.23 (broad s,1H,ArOH).

Step 8:

(1'S,1S,3R)-Methyl (5,10-dioxo-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexo-pyranose)-7-hydroxy-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone

The titled compound was prepared by applying the same procedure as described in step 8 on the 1'S, 1S, 3R, quinone glycoside of step 1 of this example.

^{1}H NMR (250 MHz, Acetone-d_6): 1.32 (d,3H,J=6.4Hz,CH_3),2.08 (m,1H, 2'-CH_2), 2.51 (m,1H,2'-CH_2) 2.55 (dd,1H,J=11.5,19.5Hz,HCHa), 2.96 (dd,1H,J=4.2,19.6Hz,HCHe), 4.51-4.62 (m,1H,3'-CH), 4.68 (dd,1H,J= 4.2,11.5Hz,0-CH-$COCH_3$), 5.52 (broad s,1H,4'-CH), 5.73 (broad s,1H, 1'-CH), 6.18 (s,1H,O-CH-O), 7.28 (dd,1H,J=2.6,8.5Hz,ArH), 7.47 (dd, 1H,J=2.6,8.5Hz,ArH), 8.03 (d,1H,J=8.5Hz,ArH), 8.38 (m,4H,ArH), 8.68 (broad d,1H,NH), 9.85 (broad s,1H,ArOH).

Step 9:

(1'S,1S,3R)-Methyl (5,10-dioxo-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-7-hydroxy-3,4,5, 10-tetrahydro [2,3-C] pyran-3-yl) ketone BCH-1180

Application of the hydrolysis procedure described in step 3 of this example to the 1'S, 1S, 3R tricyclic glycoside of step 11 resulted in the removal of the p-nitrobenzoyl protecting group. The titled compound had:

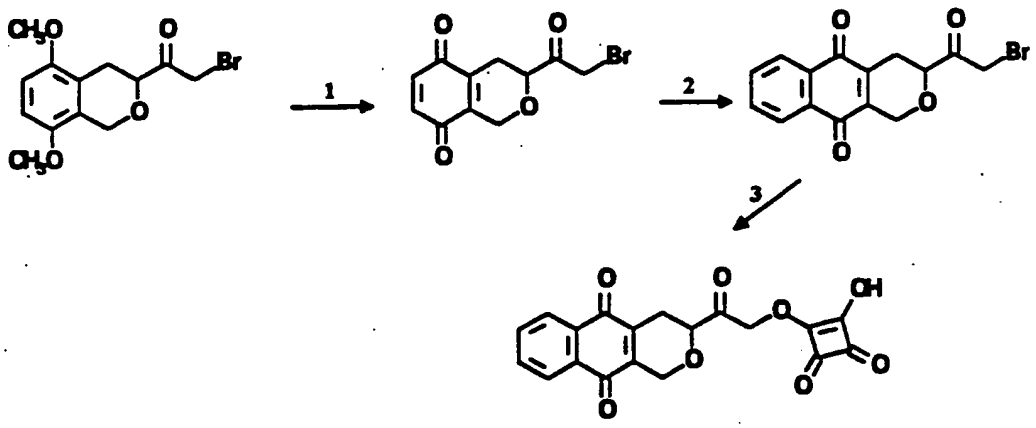
^{1}H NMR (250 MHz, Acetone-d_6) 1.73 (d,3H,J=6.6Hz,CH_3), 2.17 (m,1H, 2'-CH_2), 2.58 (m,1H,2'-CH_2), 2.68 (s,3H,$COCH_3$), 2.90 (dd,1H,J=11.6, 19.7Hz,HCHa), 3.33 (dd,1H,J=4.3,19.8Hz,HCHe), 4.09 (broad s,1H,4'-CH), 4.63 (m,1H,3'-CH), 4.95-5.06 (overlapped m,2H,5'-CH, and OCH-$COCH_3$),

5.91 (broad d,1H,1'-CH), 6.51 (s,1H,0-CH-0), 7.65 (dd,1H, J=2.6,8.5Hz,ArH), 7.85 (d,1H,J=2.6 Hz,ArH), 8.38 (d,H,J=8.5Hz, ArH), 8.52 (broad d,1H,NH), 10.18 (broad s,1H,ArOH).

EXAMPLE 6

2-[4,-Hydroxy-1',2'-dioxo-3'-cyclobutenoxy] methyl-(5,10-dioxo-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone

Example 6: Tricyclic pyranylnaphthoquinones with a squaric acid moiety.



Step 1: Bromomethyl (5,8-dioxo-5,8-dihydrobenzo [2,3-C] pyran-3-yl) ketone

To a solution containing one equivalent of 5,8-dimethoxy-3-bromoacetoisochroman (380mg,1.1mmol) in acetonitrile (18ml), at 0°C under argon, was added dropwise an aqueous solution of ceric ammonium nitrate (6.5g in 28ml H_2O). After stirring for 10 minutes, the mixture was extracted with 3 x 20ml of CH_2Cl_2. The combined organic layer was dried over $MgSO_4$ and then evaporated to yield 263 mg of pure titled compound.

^1H NMR (250 MHz,$CDCl_3$): 2.43-2.69 (m,1H,CH_2), 2.82-3.07 (m,1H,CH_2), 4.24 (dd,2H,CH_2Br), 4.4-4.6 (m,2H,CH_2O and $CHCOCH_2Br$), 4.52 (d,1H, CH_2O), 6.74 (dd,2H,HC=CH).

Step 2: Bromomethyl (5,10-dioxo-5,10-dihydronaphtho [2,3-C] pyran-3-yl) Ketone

To a solution containing one equivalent of isochromandione (263mg, 0.92mmol) from step 1 (example 6) in 25ml of dry toluene was added three equivalents (2.7mmol) of acetoxybutadiene. The reaction mixture was stirred overnight under argon at room temperature and then two hours at 60°C. After removal of solvent, the crude product was flash chromatographed (toluene/EtOAc,9:1). The titled orange compound was isolated (192mg) in 62% yield.

^1H NMR (250 MHz,$CDCl_3$): 2.4-2.6 (m,1H,CH_2), 2.7-3.2 (m,1H,CH_2), 4.3-4.4 (m,2H,CH_2Br), 4.45

(m,1H,CH-O), 4.6-4.7 (m,1H,CH_2O), 4.9-5.05 (m,1H,CH_2O), 7.6 (m,2H,ArH), 8.1 (m,2H,ArH).

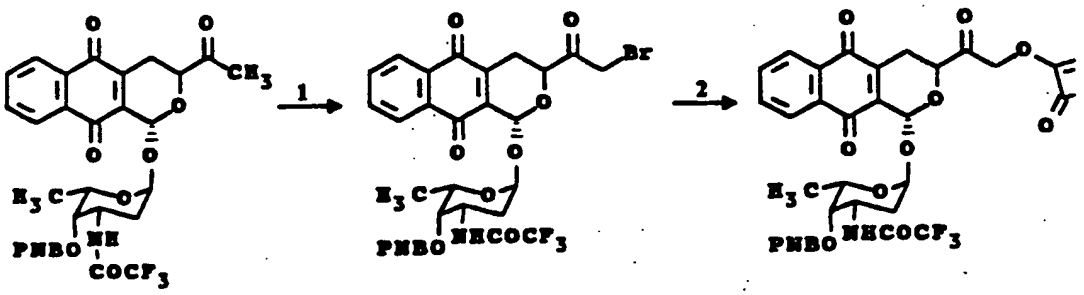
Step 3: 2-[4'-Hydroxy-1',2'-dioxo-3'-cyclobutenoxy] methyl (5,10- dioxo-3,4,5,10-tetrahydro [2,3-C] pyran-3-yl) ketone

Under argon at room temperature, two equivalents (0.9mmol) of squaric acid and two equivalents of $CsCO_3$ (0.9mmol) were disolved in 10ml of dry dimethyl formamide (DMF) (non homogeneous solution). To this solution was added one equivalent (0.45mmol) of the pyranonaphthoquinone from step 3 (example 6). The solution was treated at 60°C for two hours. After cooling, 10ml of H_2O was added, and extraction was carried out with 3 x 10ml ETOAc. After drying and evaporation, the residue was purified twice by preparative TLC. The titled compound was obtained in 30% yield.
^1H NMR (250 MHz,Acetone-d_6): 2.5-2.6 (m,1H,CH_2), 2.8-3.0 (m,1H, CH_2), 4.4 (m,1H,CH-O), 4.6 (overlapped m,2H,$COCH_2O$), 4.8-5.0 (m,2H, CH_2O), 7.7 (m,2H,ArH), 8.1 (m,2H,ArH).

EXAMPLE 71

Tricyclic pyranylnaphthoquinone glycosides with a squaric acid side chain

Example 7: Tricyclic pyranylnaphtoquinone glycosides with a squaric acic moiety.



+ 1,3-diepimer + 1,3-diepimer + 1,3-diepimer

Step 1: (1'S,1R,3S) and (1'S,1S,3R)-Bromomethyl (5,10-dioxo-1-(2',3',6'-trideoxy-4'-O-P-nitrobenzoyl-3'-trifluoro acetamido-L-lyxohexopyranose)-(3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone

At room temperature, under N_2, to one equivalent (0.482 mmol) of a 1:1 mixture starting quinone glycosides from steps 3 and 6 (example 1) dissolved in 6 ml dry tetra hydro furan (THF) was added 1.1 equivalent of pyridinium hydrobromide perbromide. After two hours, to the solution was added 7 ml 5% $NaHCO_3$ solution and extracted with 3 x 10 ml EtOAc. After drying over Na_2SO_4 and evaporation, the residue was chromatographed using 95% toluene -5% EtOAc solvent. Two major fractions were isolated corresponding to the 2 isomers (yield 40% of pure compounds, ratio # 1/1 isomer). PMRs of the separated isomers are described in step 1 (example 8) and step 1 (example 9).

Step 2:

(1'S,1R,3S) and (1'S,1S,3R)-2-[4'-hydroxy-1',2'-dioxo-3'-cyclobutenoxy] methyl (5,10-dioxo-1-[2",3",6"-trideoxy-4"-O-p-nitrobenzoyl-3"-trifluoroacetamido-L-lyxohexopyranose]-3,4,5,10-tetrahydronaphtho [2,3,c] pyran-3-yl) ketone

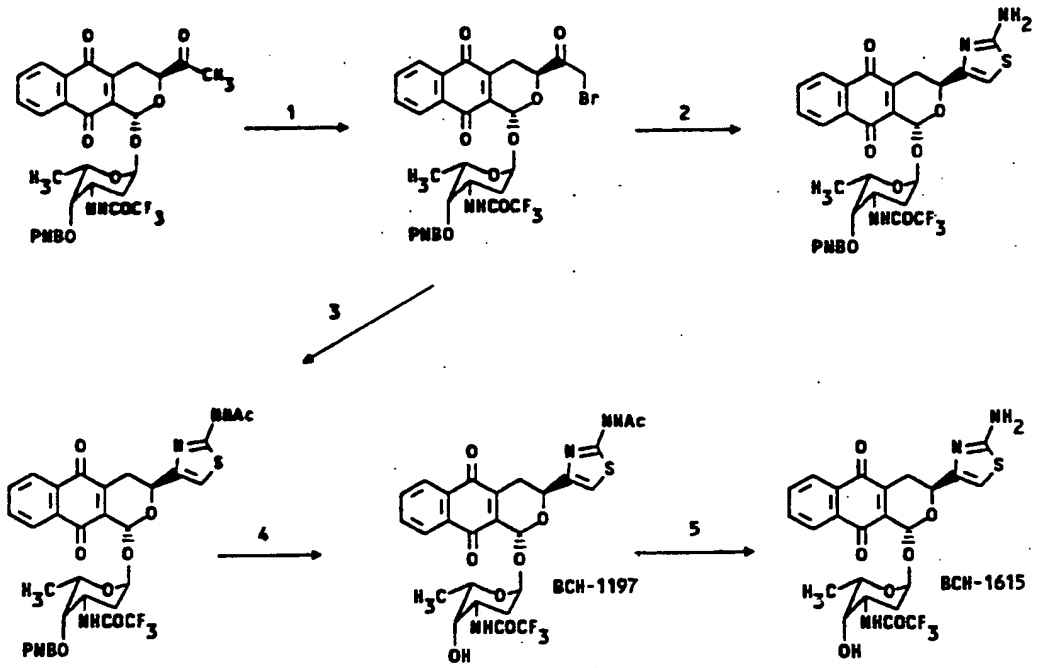
The title compounds were obtained by applying the procedure described in step 4 (example 6) to the tricyclic glycosides from step 1 (example 7).

^{1}H NMR (250 MHz, CD_3OD): 1.2 (d,3H,5"-CH_3), 1.9 (dd,1H,2"-CH_2), 2.42 (m,1H,2"-CH_2), 4.6 (m,2H,CO-CH_2-O), 4.8 (m,1H,OCH-CO), 5.5 (m, 1H,4"-CH), 5.8 (m,1H,1"-CH), 6.1 (m,1H,O-C_1H-O), 7.7-7.9 (m,2H, arom H), 8.05-8.1 (m,2H, arom H), 8.3-8.45 (m,4H, arom H), 8.7 (broad d, 1H,NH), 3.1 (m,1H,C_4-H), 2.6 (m,1H,C_4-H), 4.6-4.2 (overlapped m, 2H, 3"-CH and 5"-CH).

EXAMPLE 8

Step 1: (1'-S, 1-R, 3-S)-1-(2'-3'-6'-trideoxy-4'-p-nitrobenzoyl-3'-trifluoroacetamido-L-lyxohexopyranose)-3-(2-bromo-acetyl)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-(2,3-c)-pyran

Example 8



This example exemplifies interconversion of functional groups wherein a methyl ketone; at R_6 is eventually converted to a substituted thiazole ring.

Step 1

To a solution of (1'-S,1-R,3-S)-1-(2',3',6'-trideoxy-4'-p-nitro-benzoyl-3'-trifluoroacetamido-L-lyxohexopyranose)-3-acetyl-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-(2,3-c)-pyran (87 mg, 0.135 mmole) in tetrahydrofuran (THF) (4.5 ml), stirred at room temperature, was added slowly a solution of pyridinium hydrobromide perbromide (43.1 mg, 0.136 mmole) in 3 ml of THF. The resulting yellow liquid was stirred for 2 hours at room temperature, then poured into water. Methylene chloride was used to extract the crude product from the aqueous layer. The combined methylene chloride extracts were washed with brine (10 ml) then dried over anhydrous sodium sulfate. The organic solvent was evaporated and the crude product was obtained as a orange oil (98 mg). Chromatographic purification (by volume, ethyl acetate:toluene ~ 1:5) of the crude product gave a yellow sticky solid (40 mg) as a pure compound. A mixture (48 mg) containing the product (>34% mol) and unreacted starting material (<66% mol) was also obtained.

M.P. (Electrothermal IA-9100): 125-130°C; decomposed at 175°C.

^{1}H NMR (250MHz, acetone-d_6):1.25 (d,3H,J=6.5Hz,6'-CH_3), 1.97 (dd, 1H,J=4.8Hz,13.7Hz,2'-HCHa), 2.48 (dt,1H,J=4.2Hz,13.7Hz,2'-HCHe), 2.64 (dd,1H,J=11.6Hz,25.6Hz,4-HCHa), 3.14 (dd,1H,J=5.7Hz,25.6Hz,4-HCHe), 4.66 (S,2H,$COCH_2Br$), 4.71 (qua,1H,J=6.5Hz,5'-CH), 4.83 (overlapped m,1H,3'-CH), 5.08 (dd, 1H, J=5.7Hz,11.6Hz,3-CH), 5.52 (bs,1H,4'-CH), 5.79 (bd,1H,J=3.0Hz,1'-CH), 6.10 (S,1H,1-CH), 7.90 (m,2H,7,8-ArH), 8.08 (m,2H,6,9-ArH), 8.36 (d,2H,J=7.4Hz,PNB-COC $(CH)_2$), 8.41 (d,2H,J=7.4Hz,PNB-$NO_2C(CH)_2$), 8.75 (d,1H,J=7.7Hz,3'-$NHCOCF_3$).

IR(Nicolet 205 FT, film on Nacl tablet), cm^{-1}, 3625.9 (br,w), 3346.4 (str) 3079.5, 2955.5, 1732.6 (str), 1665.4 (str), 1596.0, 1530.9, 1274.5 (str), 1173.7, 1100.1, 974.04, 959.33 (m), 875.28, 721.29 (m).

Step 2: (1'S,1-R,3-S)-1-(2',3',6'-trideoxy-4'-p-nitrobenzoyl-3'-trifluoroacetamido-L-lyxohexopyranose)-3-(2-aza-3-aminothiazolyl)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-(2,3-c)pyran

To a suspension of thiourea (2.2mg, 0.027 mmole) in ether (2 ml) was added a solution of bromomethyl ketone (20 mg, 0.026 mmole), from the previous step in methylene chloride (1 ml). The reaction mixture was stirred at room temperature for 20 minutes when a newly formed white suspension was observed. The reaction mixture was further stirred for 3 hours.

Solvents were removed under reduced pressure to give a white solid which was treated with saturated sodium bicarbonate aqueous solution and extracted with methylene chloride (4x3 ml). The organic layer was dried (over sodium sulfate) and evaporated to give a crude product which was chromatographed (by volume, chloroform:methanol 100:3, with one drop of pyridine) to yield the titled substance (3.5 mg) as a light colored solid.

M.P. (Electrothermal IA-9100): 142°C (decomposed). ^{1}H NMR (250 MHz, acetone-d_6), δ: 1.13 (d,3H,J=6.7Hz,6'-CH_3), 1.92 (dd,1H,J=5.4Hz, 12.8Hz,2'-HCHa), 2.42 (dt,1H,J=3.4Hz,12.8Hz,2'-HCHe), 2.71 (dd,1H, J=12.2Hz,20.3Hz,4-HCHa), 3.12 (dd,1H,J=3.4Hz,20.3Hz,4-HCHe), 4.65

(m,1H,3'-CH), 4.67 (qua,1H,J=6.7Hz,5'-CH), 5.18 (dd,1H,J=3.4Hz, 12.2Hz,3-CH), 5.50 (bs,1H,4'-CH), 5.68 (d,1H,J=2.7Hz,1'-CH), 5.99 (s,1H,1-CH), 6.67 (S,1H,thiazole-CH), 7.90 (m,2H,7,8-ArH), 8.11 (m,2H,6,9-ArH), 8.35 (d,2H,J=9.4Hz,PNB-COC(CH_2), 8.42 (d,2H,J=9.4 Hz, PNB-$NO_2C(CH)_2$).

IR (Nicolet 205 FT, film on NaCl plate): cm^{-1}, 3455.4 (w), 3346.8 (str), 3119.6 (w), 2923.8, 2850.3, 1731.5 (str), 1665.0 (str), 1532.2 (str), 1273.4 (str), 1217.5, 1182.5 (m), 1161.5 (m), 1101.8, 1005.5, 957.36 (m), 874.2, 721.18 (m).

Step 3: (1'S,1-R,3-S)-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-p-nitrobenzoyl-L-lyxohexopyranose)-3-(2-aza-3-acetamidothiazolyl)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran

A solution of bromomethyl ketone (10mg, 8mmol), from step 1 (example 8), in methylene chloride (0.5 ml) was added to an ether solution (2 ml) of 1-methylthiourea (1.1mg, 1.0 mmol). The reaction mixture was stirred for 3 hours at room temperature then 3 hours at 40°C. Solvent was evaporated and the crude product was analyzed by ^1H NMR to see if the reaction was incomplete. The reaction mixture was redissolved in methylene chloride (0.5 ml) and ether (4 ml) and then stirred with newly added 1-acetylthiourea (1 mg, 1.0 mmol) and sodium iodide (0.06 mg, 0.05 mol. eqv.) at 40°C for 1 hour. Solvent was evaporated to give a crude product which was chromatographed (Eluent in volumn ratio, chloroform:methanol 20:1, with 1 drop of pyridine) to yield the title substance as a light colored solid (6 mg).

M.P. (Electrothermal IA-9100): 145-150°C, decomposed at 195°C.

^1H NMR (250 MHz, acetone-d_6), δ: 1.09 (d,3H,J=7.4Hz,6'-CH_3), 1.92 (dd,1H,J=4.7Hz,12.1Hz,2'-HCHa), 2.42 (dt,1H,J=2.3Hz,12.1Hz,2'-HCHe), 2.75 (dd,1H,J=11.7Hz,19.5Hz,4-HCHa), 3.14 (dd,1H,J=2.3Hz, 19.5Hz,4-HCHe), 4.62 (qua,1H,J=7.4Hz,5'-CH), 4.64 (m,1H,3'-CH), 5.31 (dd,1H,J=2.3Hz,11.7Hz,3-CH), 5.47 (bs,1H,4'-CH), 5.68 (bs,1H, 1'-CH), 6.00 (s,1H,1-CH), 7.20 (s,1H,thiazole-CH), 7.90(m,2H,7.8-ArH), 8.11 (m,2H,6.9-ArH), 8.34 (d,2H,J=7.8Hz,PNB:CO-C-$(CH)_2$), 8.40 (d, 2H,J=7.8Hz,PNB:NO_2-C-$(CH)_2$), 8.72 (d,1H,J=7.4Hz, 3'-NHCOCF_3), 11.08 (S,1H,thiazole-NHAc).

IR (Nicolet 205 FT, film on NaCl plate): 3539.7 (br,w), 3296.1 (str), 3083.7, 2919.4 (str), 1732.7 (str), 1667.5 (str), 1593.9 (w), 1545.7 (str), 1528.7 (str), 1127.1 (str), 1217.2, 1183.2, 1166.2, 1104.0, 1008.9, 975.46, 956.53, 718.14 (m).

Step 4: (1'-S,1-R,3-S)-1-(2',3',6'-trideoxy-3'-trifluoro acetamido-L-lyxohexopyranose)-3-(2-aza-3-acetamido thiazolyl)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran

To an ice-cold solution of PNB-derivative (3mg, 4.1 mmol), from the previous step, in a tri-solvent system containing water (98 μl), MeOH (422 μl) and methylene chloride (158 μl) was added an aqueous

solution (20 μl) of sodium bicarbonate (0.51 mg, 6.11 mmol). The reaction mixture was then stirred at room temperature for 1 hour. When the reaction was completed, (as judged by thin-layer-chromatography), the reaction mixture was poured into a bi-layer system of methylene chloride and saturated aqueous ammonium chloride solution (5 ml/5 ml). The well-shaken mixture was then allowed to settled and the organic layer was separated, dried over sodium sulfate, and evaporated to give the titled substance as a light colored solid (1.4 mg).

M.P. (Electrothermal IA-9100): 160-165°C, decomposed at 195°C.

^{1}H NMR (250 MHz, acetone-d_6), δ: 1.12 (d,3H,J=7.9Hz,6'-CH_3), 1.24 (dd,1H,J=6.7Hz,15.0Hz,2'-HCHa), 2.14 (dt,1H,J=4.2Hz,15.0Hz,2'-HCHe), 2.25 (s,3H,$COCH_3$), 2.64 (dd,1H,J=12.5Hz,20.9Hz,4-HCHa), 3.13 (dd,1H,J=4.2Hz,20.9Hz,4-HCHe), 3.63 (bs,1H,4'-CH), 4.21 (qua,1H, J=7.9Hz, 5'-CH), 4.30 (m,1H,3'-CH), 5.26 (dd,1H,J=4.2Hz,12.5Hz,3'-CH), 5.50 (d,1H,J=2.4HZ,1'-CH), 5.97 (s,1H,1-CH), 7.12 (s, 1H, thiazole-CH), 7.90 (m,2H,7.8,ArH), 8.10 (m,2H,6.9,ArH), 11.07 (s,1H,thiazole-NHAc).

IR (Nicolet 205 FT, film on NaCl plate): 3668.0-3119.7 (peaked at 3268.3,br,str), 3073.7 (w), 2925.1, 1711.8 (str), 1669.4 (str), 1591.6 (w), 1549.1, 1375.8, 1290.9 (str), 1170.6, 1006.5 (w), 984.49(str), 716.33 (w).

Step 5: (1'-S,1-R,3-S)-1-(2',3',6'-trideoxy-3'-trifluoro acetamido-L-lyxohexopyranose)-3-(2-aza-3-aminothiazolyl)-5, 0-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-C] pyran

To a sample of PNB-derivative (2.5 mg, 3.5 μmol) from step 2, dissolved in a tri-solvent system containing water (85.7μl), methanol (370μl) and methylene chloride (138μl), at 0°C, was added a solution of sodium bicarbonate (0.66 mg, 7.0 μmol, in 30μl of water). The reaction mixture was stirred at room temperature for 1.5h untill a total consumption of the starting material. It was poured into a saturated sodium bicarbonate solution (4ml) and evaporated with methylene chloride (5x2ml). The organic layer was dried over sodium sulfate and then evaporated to give a crude product which was further purified by recrystalization from methylene chloride/hexane to give an off-white solid (1.5mg).

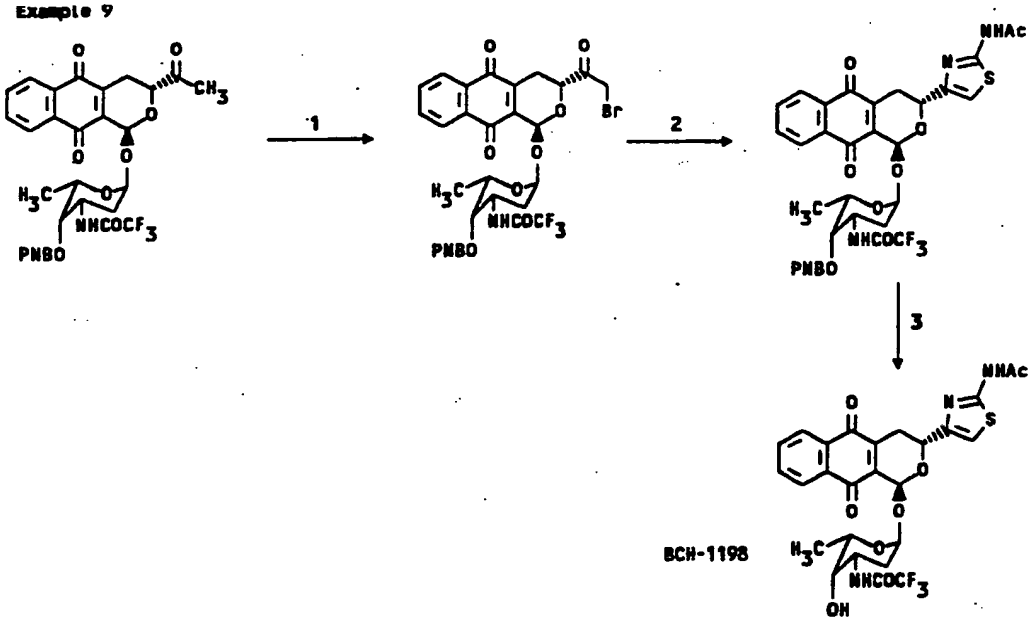
M.P. (Electrothermal IA-9100): 142-146°C.

^{1}H NMR (250 MHz, acetone-d_6), δ: 1.14 (d,1H,J=5.9Hz,6'-CH_3), 1.74 (dd,1H,J=12.5Hz,4.8Hz,2'-HCHa), 2.11 (m,1H,2'-HCHe), 2.62 (dd,1H, J=11.8Hz,18.4Hz,4'-HCHa), 3.12 (dd,1H,J=4.2Hz,18.4Hz,4-HCHe), 3.65 (bs,1H,4'-CH), 4.24 (qua,1H,J=5.9Hz,5'-CH), 4.33 (m,1H,3'-CH), 5.11 (dd,1H,J=4.2Hz,11.8Hz,3-CH), 5.48 (bd,1H,J=3.0Hz,1'-CH), 5.92 (s, 1H,1-CH), 6.57 (s,1H,thiazole-CH), 7.87 (m,2H,7.8,ArH), 8.08 (m,2H, 6.9,ArH).

IR (Nicolet 205FT, film on NaCl plate): 3423.9 (str), 3341.1 (str), 2927.0, 2853.4 (w), 1718.5 (str), 1664.4 (str), 1597.5, 1524.7, 1335.0, 1300.1 (str), 1174.0, 100.4, 984.61 (str), 724.51, 707.71.

EXAMPLE 9

Example 9



Step 1: (1'-S,1-S,3-R)-1-(2',3'-6'-trideoxy-4'-p-nitrobenzoyl-3'-trifluoro-acetamido-L-lyxohexopyranose)-3-(2-bromoacetyl)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran

To a solution of (1'-S,1-S,3-R)-1-(2',3',6'-trideoxy-4'-p-nitrobenzoyl-3'-trifluoroacetamido-L-lyxohexopyranose)-3-acetyl-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran (50 mg, 0.077 mmol) in tetrahydrofuran (3 ml), stirred at room temperature, was added a solution of pyridinium hydrobromide perbromide (24.5 mg, 0.077 mmol) in THF. The reaction mixture was stirred for 2 hours at room temperature, then poured into water (10 ml) and extracted with methylene chloride (3x5 ml). The combined organic extracts were washed with brine (5 ml), and dried over sodium sulfate. The solvent was evaporated to give a crude product (68 mg) from which, via flash chromatography (eluent in volume ratio, toluene:ethyl acetate 10:3), a pure sample of the titled substance (27 mg) was obtained as a light yellow solid. Unreacted starting material (10 mg) was also obtained.

^{1}H NMR (250 MHz,acetone-d_6), δ: 1.33 (d,3H,J=6.8Hz,6'-CH_3), 2.02 (dd, 1H,J=4.9Hz,13.5Hz,2'-HCHa), 2.48 (dt,1H,J=5.8Hz,13.5Hz,2'-HCHe), 2.78 (dd,1H,J=12.1Hz,20.3Hz,4-HCHa), 3.12 (dd,1H, J=4.0Hz, J=20.3 Hz,4-HCHe), 4.29 (m,1H,3'-CH), 4.52 (d,1H,J=13.8Hz,BrHCHre), 4.67 (d,1H,J=13.8Hz,BrHCHsi), 4.88 (qua,1H,J=6.8Hz,5'-CH), 5.04 (dd,1H, J=4.0Hz,12.1Hz,3-CH), 5.53 (bs,1H,4'-CH), 5.85 (bd,1H,J=3.4Hz,1'-CH), 6.24 (s,1H,1-CH),7.90 (m,2H,7,8-ArH), 8.10 (m,2H,6,9-ArH), 8.48 (qua-like m,4H,PNB-ArH), 8.70 (bd,1H,J=7.4Hz,3'-$NHCOCF_3$).

Step 2: (1'-S,1-S,3-R)-1-(2',3'-6'-trideoxy-4'-O-p-nitrobenzoyl-3'-trifluoroacetamido-L-lyxohexopyranose)-3-(2-aza-3-acetamido)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran

A sample of 1-acetylthiourea (1.06 mg, 9.0 mmol) in ether (2 ml) was stirred at room temperature while a solution of bromomethyl ketone (9 mg, 8mmol), from the previous step, in methylene chloride (0.5 ml) was added. The resulting mixture was stirred for 3 hours at room temperature and then for 4 hours at 40°C. Solvent was evaporated to give a crude product which was purified via flash chromatography (eluent in volume ratio chloroform:methanol~100:7, with 1 drop of pyridine added), to yield a product, which was further purified by recrystallization from CH_2Cl_2/hexane. The titled substance was obtained as an off-white solid (4mg).

^1H NMR (250 MHz, acetone-d_6), δ: 1.33 (d,3H,J=7.5Hz,6'-CH_3), 1.96 (dd,1H,J=5.8Hz,15.2Hz,2'-HCHa), 2.28 (s,3H,$COCH_3$), 2.49 (dt,1H, J= 3.8Hz,15.2Hz,2'-HCHe), 2.76 (dd,1H,J=12.5Hz,20.0Hz,4-HCHa), 3.15 (dd,1H,J=4.2Hz,20.0Hz,4-HCHe), 4.60 (m,1H,3'-CH), 4.92 (qua,1H, J=7.5Hz,5'-CH), 5.24 (dd,1H,J=4.2Hz,12.5Hz,3-CH), 5.55 (bs,1H,4'-CH), 5.68 (bd,1H,J=3.0Hz,1'-CH), 6.16 (s,1H,1-CH), 7.18 (s,1H, thiazole-CH), 7.92 (m,2H,7,8-ArH), 8.14 (m,2H,6,9-ArH), 8.36 (d,2H, J=8.3Hz,PNB-OCOC$(CH)_2$), 8.42 (d,2H,J=8.3Hz,PNB-$NO_2C(CH)_2$), 8.74 (bd, 1H,J=7.9Hz, 3'-NHCOCF_3), 11.07 (s,1H,thiazole-NHAC).

Step 3: (1'-S,1-S,3-R)-1-(2',3',6'-trideoxy-3'-trifluoro acetamido-L-lyxohexopyranose)-3-(2-aza-3-acetamido-thiazolyl)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran

A sample of the PNB-derivative (4.0 mg, 5.5 mmol), from the previous step, was taken into a solvent system containing methylene chloride (212 μl) methanol (566 μl) and water (131 μl), and cooled to 0°C. An aqueous solution of sodium bicarbonate (0.69 mg, 8.2 mmol in 20 μl of water) was then added to the reaction mixture. The reaction proceeded at 0°C for 1 hour and at room temperature for 20 minutes. The reaction mixture was poured into a mixture of methylene chloride and saturated ammonium chloride aqueous solution (5ml/5ml). The organic layer was separated, dried over sodium sulfate and then evaporated to dryness. The crude product was recrystalized from dichloromethane/hexane to yield the titled substance as a light-colored solid.

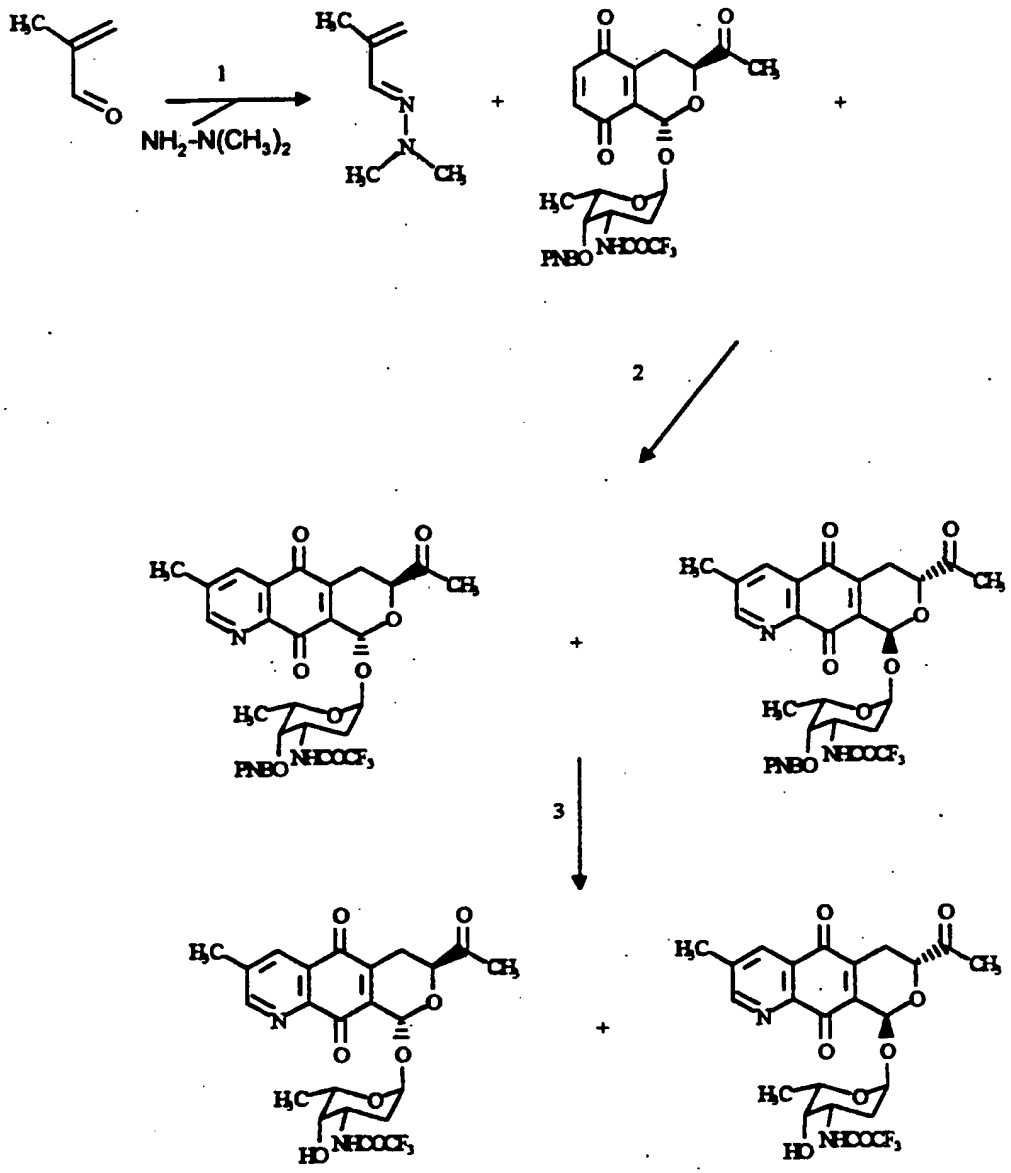
M.P. (Electrothermal IA-9100): Decomposed at 195°C.

^1H NMR (250 MHz, acetone-d_6), δ: 1.35 (d,3H,J=7.5Hz,6'-CH_3), 1.76 (dd,1H,J=5.8Hz,14.2Hz,2'-HCHa), 2.16 (dt,1H,J=4.2Hz,14.2Hz,2'-HCHe), 2.75 (dd,1H,J=12.1Hz,20.2Hz,4-HCHa), 3.12 (dd,1H,J=4.0Hz, 20.2Hz,4-HCHe), 3.72 (bs,1H,4'-CH), 4.28 (m,1H,3'-CH), 4.58 (qua,1H, J=7.5Hz,5'-CH), 5.18 (dd,1H,J=4.0Hz,12.1Hz,3-CH), 5.48 (bd,1H, J=2.9Hz,1'-CH), 6.10 (s,1H,1-CH), 7.16 (s,1H,thiazole-CH), 7.90 (m,2H,7,8-ArH), 8.11 (m,2H,6,9-ArH), 8.17 (d,1H,overlapped,3'-NHCOCF_3), 11.07 (s,1H,thiazole-NHAc).

IR (Nicolet 205 FT, film on NaCl plate): 3746-3048 (peaked at 3388.3, br,str), 2923.2, 1712.9 (str), 1664.9 (str), 1591.9, 1550.1, 1535.5 (str), 1289.3 (str), 1243.4 (m), 1145.4 (w), 1124.5, 1080.7, 1001.5, 971.57 (str), 936.11, 709.75 (w).

EXAMPLE 10

Example 10



Step 1: Methacrolein-N,N-dimethylhydrazone

Under N_2, at room temperature, was mixed 3g (50mM) of dimethylhydrazine in sodium phosphate solution 7.1g (50mM) in 50 ml H_2O and 3.5g (50mM) methacrolein. The mixture was vigorously stirred for 10 minutes at 60°C and then 30 minutes at room temperature. The solution was extracted with Et_2O

(3x40 ml), dried over $MgSO_4$, and evaporated. The residue was flash chromatographed using CH_2Cl_2 as eluent; 5.1g of colorless oil was isolated.

^1H NMR (250 MHz, $CDCl_3$)δ: 2.13 (s,3H,CH_3), 3.04 (s,6H,$N(CH_3)_2$), 5.23 (broad s,1H,C=CH_2), 5.32 (broad s,1H,C=CH_2), 7.25 (s,1H,C=CH).

Step 2: (1'S,1S,3R) and (1'S,1R,3S) methyl (1-[2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexo-pyranose]-5,10-dioxo-3,4,5,10-tetrahydro-7-methyl-9-aza naphtho [2,3-c] pyran-3-yl ketone

Under N_2 at room temperature, to 235 mg (0.394 mM) of quinone from step 1 (example 5) dissolved in 20 ml of dry THF , was added 1.1 eq. (47 mg, 0.399 mol) of hydrazone from step 1 (example 10), and 1.1 eq of p-toluene sulfonic acid (0.4 mM, 76 mg). After stirring 1 day at room temperature, the mixture was poured into 20 ml of H_2O, and extracted with EtOAc (3x15 ml). After drying and evaporation, the residue was flash chromatographed [EtOAc 1: toluene 3] to give 95.1 mg of titled compound (40% yield).

^1H NMR (250 MHz, $CDCl_3$)δ: 1.22 (d,3H,5'-CH_3), 1.75 (dd,1H,2'-CH_2), 2.18 (m,1H,2'-CH_2), 2.32 (s,3H,$COCH_3$), 2.59 (s,3H,C_7-CH3), 2.62 (overlapped m,1H,H-C_4-H), 3.1-3.3 (m,1H,HC_4H), 4.32 (m,1H,5'-CH), 4.53 (m,1H,C<u>H</u>$COCH_3$), 5.4 (m,1H,3'-CH); 5.5 (m,1H,4'-CH), 5.7 (m,1H, 1'-CH), 6.2 (s,1H,C_1-H); 6.4 (m, broad,1H,NH), 8.2 (overlapped m, 1H,C_6-H-arom), 8.2-8.4 (m,4H,p-nitobenzoyl), 8.2 (m,1H,C_8-H arom).

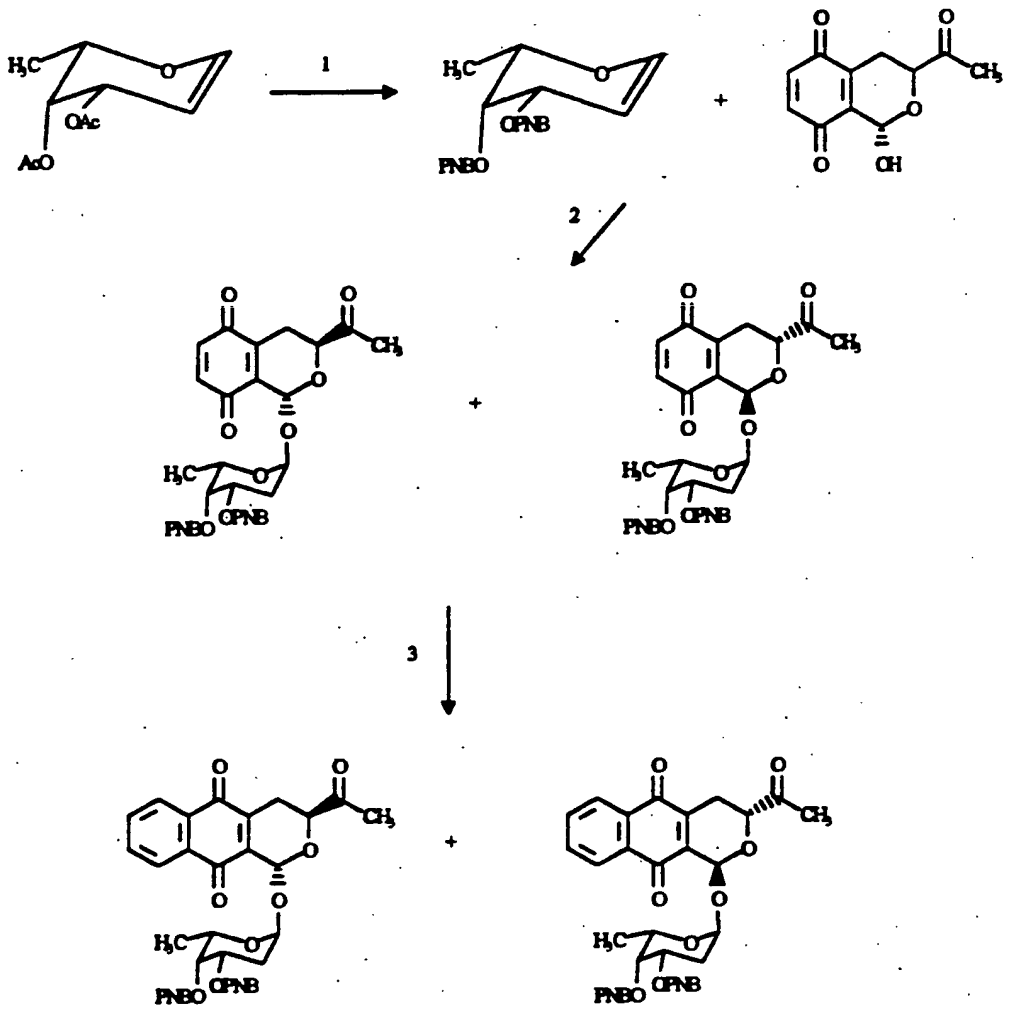
Step 3: (1'S,1S,3R) and (1'S,1R,3S) methyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-hydroxy-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10-tetrahydro-7-methyl-O-azanaphtho [2,3-c] pyran-3-yl ketone

To 80 mg (0.121 mM) of azaquinone from step 2 (example 10), dissolved in 13 ml MeOH and 3.2 ml H_2O, was added 10.4 mg (0.121 mM) of $NaHCO_3$. After stirring for 2 hours, the reaction was over, and 15 ml of H_2O was added. The mixture was extracted with 3x15 ml EtOAc. After drying and evaporation, the residue was purified by preparative TLC and yielded 30.4 mg of pure titled compounds (50% yield).

^1H NMR (250 MHz, $CDCl_3$)δ: 1.24 (d,3H,J=6.5Hz,CH_3), 1.76 (dd,1H,2'-CH_2), 2.16 (m,1H,2'-CH_2), 2.30 (s,3H,$COCH_3$), 2.58 (s,3H,C_7-CH_3), 4.3 (m,1H;5'-CH), 4.52 (m,1H,C<u>H</u>-$COCH_3$), 5.3 (dd,1H,3'-CH), 5.5 (dd,1H, 4'-CH), 5.6 (m,1H,1'-CH), 6.1 (s,1H,C_1-H), 6.4 (m, broad, 1H,NH), 8.2 (m,1H,C_6-H arom), 8.9 (m,1H, C_8-H arom).

EXAMPLE 11

Example 11 Preparation of naphto[2,3-C] pyran glycosides of 2-deoxyfucose.



Step 1: Di-p-nitrobenzoyl-L-fucal

To a stirred solution of diacetyl-L-fucal (114 mg, 0.53 mmol) in methanol (2.5 ml) was added a solution of sodium methoxide in methanol (25µl, 4.37 M, 0.1 mmol) after 45 minutes, methanol was evaporated under vacuum. The crude product was dissolved in CH_2Cl_2 (2.5 ml) and pyridine (1.5 ml) and at 0°C, p-nitrobenzoyl chloride (2.1 mmol, 390 mg) was added. After a few minutes at 0°C, the reaction mixture was poured in CH_2Cl_2 (20 ml) and washed with water, $NaHCO_3$ 10%, and then brine. The titled product was purified by flash chromatography (hexanes/acyl acetate (AcOet 5:1)) (MP: 130-132°C) (210mg, 90%).

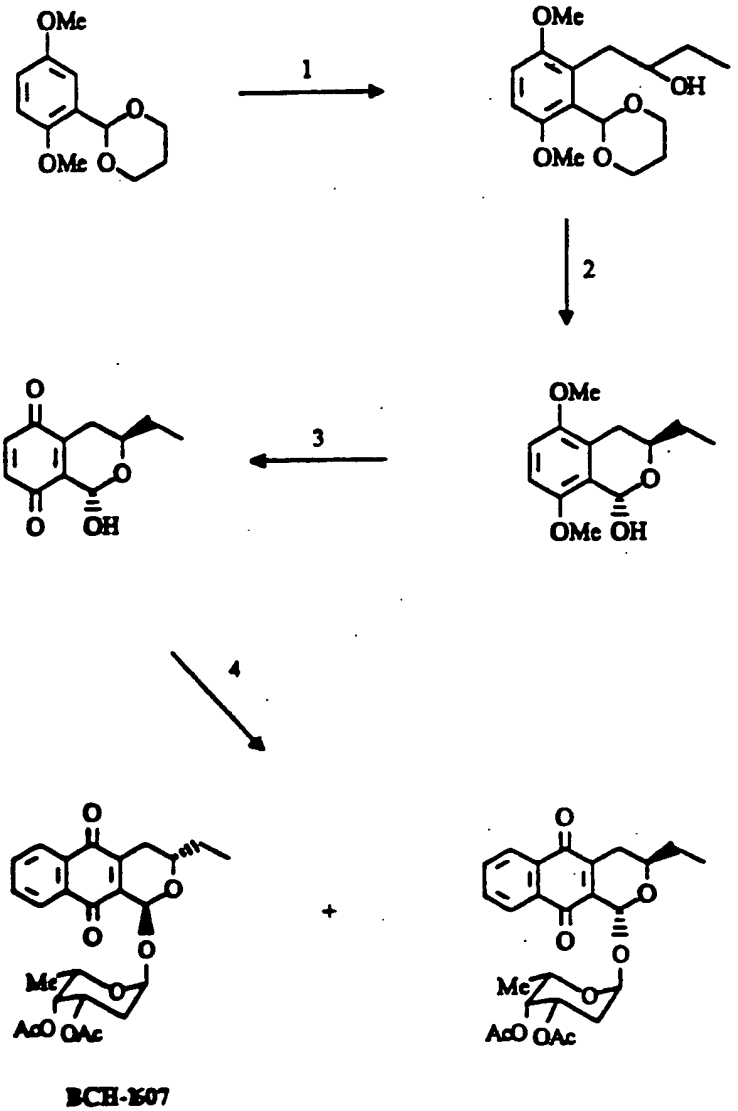
^1H NMR (250 MHz, CD_2Cl_2)δ: 1.40 (d,3H,-CH_3), 4.40 (q,1H,H-5), 4.85 (m,1H,H-2), 5.65 (m,1H,H-4), 5.90 (m,1H,H-3), 6.6 (m,1H,H-1).

Step 2:

(1'S,1S,3R) and 1'S,1R,3S)-methyl-1-(2',6'-dideoxy-3',4'-di-O-p-nitrobenzoyl-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone

To a mixture of methyl (1-hydroxy-5,8-dioxo-5,8-dihydroisochroman-3-yl) ketone (698 mg, 3.1 mmol), 1,5-anhydro-3,4-di-O-para-nitrobenzoyl-2,6-dideoxy-L-lyxohex-1-enitol (1.58g, 3.7 mmol), and molecular sieves 4 °A (3.8g) in CH_2Cl_2 (150 ml), at -60°C, was added triethylamine (0.24 ml, 1.7 mmol), and trimethylsilyl trifluoromethanesulfonate (0.64 ml, 3.3 mmol), subsequently. After stirring for 40 minutes, the reaction was quenched by adding aqueous $NaHCO_3$ (50 ml) at -60°C and gradually warmed up to room temperature. Insolubles were filtered off and the filtrate was extracted into CH_2Cl_2. The organic phase was washed with aqueous HCl (0.1N), 100ml, water and brine, dried over $MgSO_4$ and the solvent evaporated to give 2.36 g of crude isochromandione glycoside. This was used without any further purification. To a solution of the quinone (mixture of diastereomers: 0.16g, 0.25 mmol) in 2.5 ml of dry toluene, under argon at room temperature, was added 1-acetoxybutadiene (0.15 ml, 5 eq) and the reaction mixture was stirred for 18 hours. Silica gel (1.0 g) was then added and air was bubbled through the suspension. After 15 minutes, the mixture was chromatographed (silica gel, 3:1 hexanes/ethyl acetate) to give 0.13 g (74%) of compound 178-24-01 (1:1 mixture of diastereomers) as a yellow solid:mp. 129-132. ^1H NMR ($CDCl_3$)δ: 8.34-7.73 (m,12H), 6.23+6.06 (2s,1H), 5.82+5.72 (2d,1H,J=2.8), 5.62-5.52 (m,2H), 4.88+4.43 (2q,1H,J=6.5), 4.62+4.58 (2dd,1H,J=4.1,11.5), 3.10+3.02 (2dd,1H,J=4.1,6.1), 2.62-2.10 (m,3H), 2.35+2.33 (2s,3H), 1.42+1.28 (2d,3H,J=6.5).

EXAMPLE 12



BCH-1607

Step 1: 2,5-Dimethoxy-6-(2-hydroxybutyl)-benzaldehydedioxane acetal

To a cooled (-15°C) solution of 2,5-dimethoxybenzaldehydedioxane acetal (13.2 g; 44.6 mmol) in 300 ml of anhydrous diethylether was added dropwise, under argon, n-Butyllithium (32.2 ml of a 2.5M solution in hexanes, 80.3 mmol). The mixture was warmed to -7°C and was stirred at this temperature for 5 hours. The resulting mixture was cooled to -78°C, treated with boron trifluoride etherate (21.8 ml; 177 mmol), and 1,2 epoxybutane (10.2 ml; 119 mmol). After stirring at -78°C for 60 minutes the reaction mixture was quenched with a saturated solution of bicarbonate and then extracted with ether. The organic

layers were combined, washed with water, and brine, and were dried over $MgSO_4$. Removal of the solvent gave a crude oil which was purified by column chromatography on silica gel using 25% ethyl acetate in hexane to afford 2.39 g of pure starting material (18%) and 5.21 g (52% based on S.M. recovered) of 2,5 dimethoxy-6-(2 hydroxybutyl) benzaldehydedioxane acetal as an oil.

^1H NMR (250 MHz, $CDCl_3$)δ: 0.95 (t,J=7.3 Hz,3H,-CH_2CH_3), 1.35 (1H, dm,J=13.6Hz,-CH_2-$CH\underline{H}_{eq}$-CH_2), 1.55 (2H,m,-CH_2-CH_3), 2.18 (1H,m,-CH_2-$CH\underline{H}_{ax}$-CH_2-) 2.98 (1H,dd,J=2.7 and 13.7 Hz,=C-CH_2-CH-O-), 3.36 (1H,dd, J=10.3 and 13.6 Hz=C-CH_2-CH-O) 3.65 (3H,s,-OCH_3), 3.66 (3H,s,-OCH_3), 3.60 - 4.10 (4H,m,-$CH\underline{H}_{eq}$-O-,-C$\underline{H}$-O$\underline{H}$), 4.16 (2H,m,-$CH\underline{H}_{ax}$-O-), 6.16 (1H, s,-O-C$\underline{H}$-O-), 6.61 (1H,d,J=9.0 Hz,Ar-H), 6.70 (1H,d,J=9.0 Hz,Ar-H).

Step 2: 5,8-Dimethoxy-3-ethyl-1-hydroxy-isochroman

To a stirred solution of 2,5 dimethoxy-6-(2-hydroxybutyl) benzaldehydedioxane acetal (5.2 g; 17.6 mmol) in 700 ml of THF at room temperature was added dropwise 25 ml of a 1N solution of HCl. The resulting mixture was stirred for an hour at room temperature and then quenched with a saturated solution of sodium bicarbonate. It was then diluted with 1000 ml of dichloromethane and the aqueous layer, after separation, was extracted twice with dichloromethane. The combined organic layers were washed with brine and dried over $MgSO_4$. Evaporation of the solvent gave pure 5,8-dimethoxy-3-ethyl-1-hydroxy-isochroman (4.1 g; 98%) which could be recrystalized in dichloromethane/hexane to give white crystals (M.P.:108.9-110.1°C).

^1H NMR (250 MHz, C_6D_6)δ: 1.02 (3H,t,J=7.4 Hz,CH_2-$C\underline{H}_3$), 1.60 (1H,m, -C$\underline{H}$H-CH_3), 1.76 (1H,m,-C$\underline{H}$H-CH_3), 2.48 (1H,dd,J=11.6 and 17.3 Hz, Ar-CH-$\underline{H}_{ax}$-), 2.88 (1H,dd,J=3.3 and 17.3 Hz, Ar-CH-$\underline{H}_{eq}$), 2.98 (1H,d,J=3.9 Hz,-O$\underline{H}$), 3.34 and 3.38 (6H,2S,-O-CH_3), 4.28 (1H,m,-C$\underline{H}$-CH_2-CH_3), 6.40 (2H,m,ArH and -O-C$\underline{H}$-O-), 6.46 (1H,d,J=8.8 Hz,ArH).

Step 3: 3-Ethyl-1-hydroxy-isochroman-5,8-dione.

To a stirred solution of 5,8-dimethoxy-3-ethyl-1-hydroxy-isochroman (760 mg; 3.19 mmol) in 160 ml of acetonitrile at 0°C was added dropwise a solution of ceric ammonium nitrate (CAN) (5.25 g; 9.57 mmol) and sodium bicarbonate (1.45 g; 17.2 mmol) in 40 ml of water. The resulting mixture was stirred for an hour at 0°C and was quenched by adding a saturated bicarbonate solution. The aqueous layer was extracted 3 times with dichloromethane and the combined organic layer was washed with water, brine, and dried over $MgSO_4$. Evaporation of solvent gave a crude quinone which was suitably pure to undergo further reactions (600 mg; 90%).

^1H NMR ($CDCl_3$)δ: 1.02 (3H,t,J=7.4 Hz,-CH_2-$C\underline{H}_3$), 1.70 (2H,m,-C$\underline{H}_2$-CH_3), 2.15 (1H,ddd,J=1.1,12.4 and 19.5 Hz,Ar-CH-$\underline{H}_{ax}$-), 2.60 (1H,dd,J=3.2 and 19.5 Hz,Ar-CH-$\underline{H}_{eq}$-), 3.20 (1H,br s,-O$\underline{H}$), 4.08 (1H,m,-C$\underline{H}$-CH_2-CH_3), 5.91 (1H,s,-O-C$\underline{H}$-O-), 6.76 (2H, 2 parts of an AB system, Ar-H).

Step 4: (1'S, 1S, 3S) and (1'S, 1R, 3R)-5,10-dioxo-3-ethyl-1-(2',3',4',6'-tetradeoxy-3',4'-diacetoxy-L-lyxohexo-pyranose)-3,4,5,10-tetrahydro-1H-naphtho [2,3-C] pyran

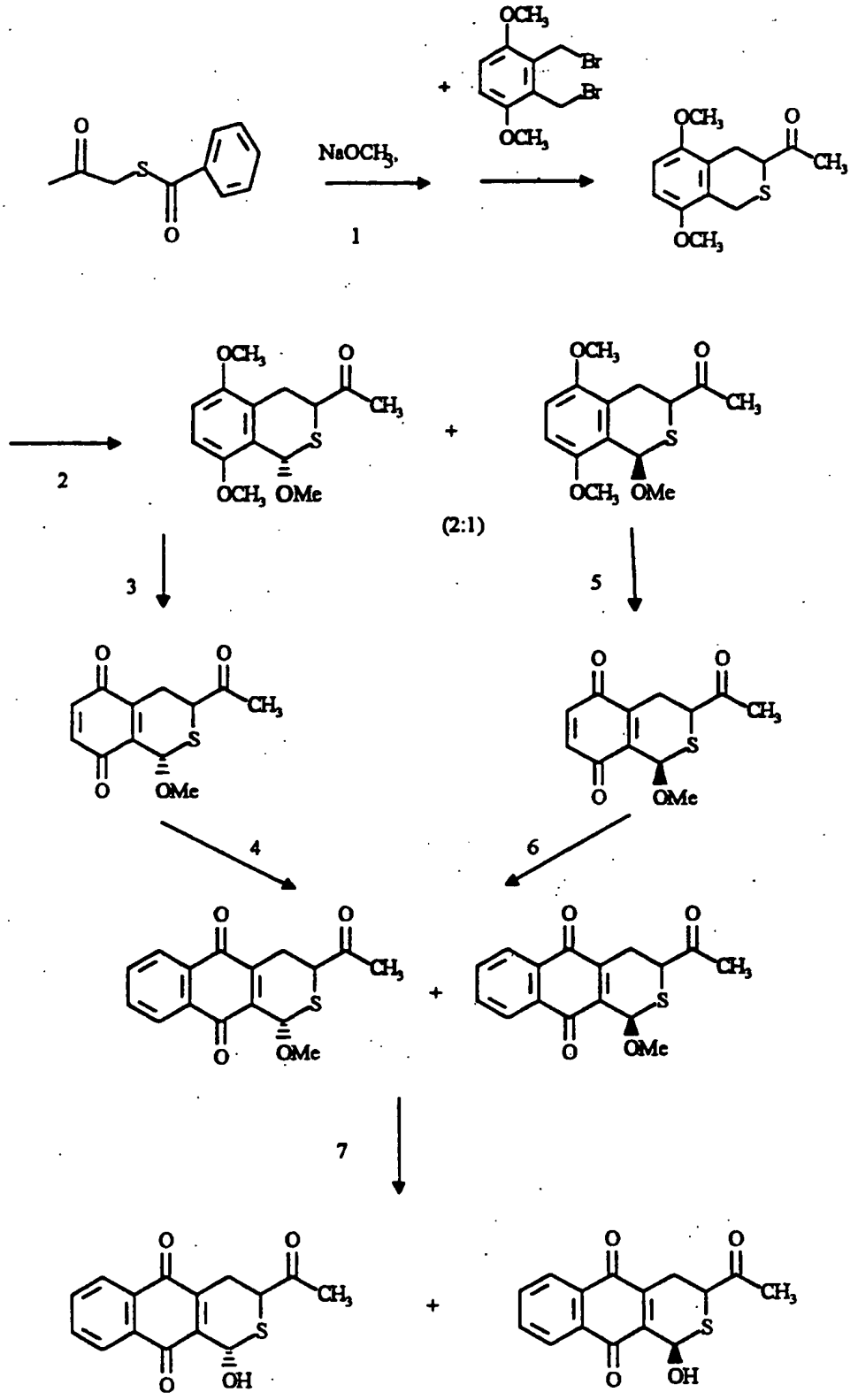
To a cooled solution (-60°C) of 3-ethyl-1-hydroxy-isochroman-5,8-dione (150 mg;.72 mmol) in dichloromethane (40 ml) were added sequentially molecular sieves (4A, 864 mg), 3,4-di-O-acetyl-L-fucal (246 mg; 1.15 mmol), triethylamine (56 μl) and trimethylsilyl trifluoromethanesulfonate (138 μl; .72 mmol). The resulting mixture was stirred at -60°C for 3 hours and was quenched with an aqueous saturated bicarbonate solution. Extraction with dichloromethane was followed by washing of the combined organic layers with 1N HCl, brine, and then drying over $MgSO_4$. Following evaporation, 407 mg of the resulting crude thick oil was dissolved in 20 ml of toluene. To this solution was added 1-acetoxy-1,3-butadiene (521 mg; 4.82 mmol) and the resulting mixture was stirred at room temperature for 18 hours. Solvent was then partially evaporated to about 4 ml volume and the residue was applied to a column of silica gel (eluent, toluene, ethyl acetate 90:10) affording 2 fractions. The first one (48 mg, 14% overall) contained a 2:1 mixture favoring the (1'S, 1S,3S)-5,10-dioxo-3-ethyl-1-(2',3',4',6'-tetradeoxy-3',4'-diacetoxy-L-lyoxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho [2,3-C] pyran over its (1'S, 1R, 3R) isomer and a second fraction (157 mg; 46% overall) consisting in a 1.5:1 mixture of the same major diastereomer that was about 80% pure from ^1H NMR analysis.

^1H NMR (1'S,1S,3S isomer, CD_2Cl_2)δ: 1.00 (3H,t,J=7.3Hz,-CH_2-CH_3), 1.23 (3H,d,J=6.4Hz,6'-CH_3), 1.55-2.20 (4H,m,-CH_2-CH_3 and H-2'), 1.89 and 2.12 (6H,2s,O=C-CH_3), 2.27 (1H,dd,J=11.3 and 19.3Hz,H_{ax}-4), 2.74 (1H,dd,J=3.3 and 19.5Hz,H_{eq}-4), 3.95 (1H,m,H-3), 4.58 (1H, q,J= 6.5 Hz,H-5'), 5.10 (2H,m,H-3'and H-4'), 5.46 (1H,d,J=3.5Hz,H-1'), 5.95 (1H,s,H-1), 7.75 and 8.05 (4H,2m,Ar-H).

^1H NMR (1'S,1R,3R isomer, CD_2Cl_2)δ: 1.01 (3H,t,J=7.3Hz,-CH_2-CH_3), 1.11 (3H,d,J=6.5Hz,6'-CH_3), 1.55-2.35 (5H,m,-CH_2-CH_3,H-2' and H_{ax}-4), 1.89 and 2.12 (6H,2s,O=C-CH_3), 2.74 (1H,dd,J=3.3 and 19.5Hz, H_{eq}-4), 4.00 (1H,m,H-3), 4.22 (1H,q,J=6.5Hz,H-5'), 5.10 (2H,m,H-3' and H-4'), 5.54 (1H,d,J=3.0Hz,H-1'), 5.79 (1H,s,H-1), 7.75 and 8.05 (4H,2m,Ar-H). The (1'S,1S,3S) diastereoisomer was obtained pure by recrystalization.

EXAMPLE 13

Example 13 Preparation of naphto[2,3-C] thiopyran aglycones.



Step 1: 3-Aceto-5,8-dimethoxythioisochroman

1-Thiobenzoate-propan-2-one (10.083g,51.97mmole) was dissolved in MeOH (100ml), cooled to 0°C, followed by the slow addition of NaOMe (4.37M,14.3ml,62.36mmol). The resulting mixture was stirred at 0°C for 3/4 hr. It was then cooled to -78°C followed by the slow addition of 2,3-dibromomethyl-1,4-dimethoxybenzene (6.74g,20.79 mmol) in CH_2Cl_2: MeOH (60:20ml). The resulting mixture was slowly warmed to R.T. and stirred for 2 1/2 hrs. NH_4Cl (saturated solution) was added and it was extracted with ethyl acetate. The combined organic phases were dried over $MgSO_4$, filtered and concentrated in vacuum. The crude obtained was flash chromatographed to give the titled compound (2.08g,8.25mmol) in 41% yield.

^1H NMR (250MHz, CD_3COCD_3)δ: 2.31 (s,3H,CH_3),2.83(dd,1H,J=1.06, 8.55 Hz, HC$\underline{H}_a$CH-S), 2.99 (dd,1H,J=2.44,6.17Hz, HC$\underline{H}_e$CH-S), 3.44 (m,1H, CH-S), 3.78 (2s,6H,OCH_3), 3.85 (2H,CH_2-S), 6.78 (dd,2H, J=8.95, 12.58Hz,ArH). IR (cm^{-1}): 2900: CH, 1707: C=O.

Step 2: Trans-3-aceto-1,5,8-trimethoxythioisochroman and cis-3-aceto-1,5,8-trimethoxythioisochroman

The thioisochroman from step 1 (Example 13) (100.0mg,0.40 mmmol) was dissolved in CH_2Cl_2 (12ml) and MeOH (4ml) followed by the addition of DDQ (109.0mg,0.48mmol,1.2eq [I]) at R.T. The resulting mixture was stirred at room temperature overnight. H_2O was added and it was extracted with CH_2Cl_2. The combined organic phases were washed with water, dried over $MgSO_4$, filtered and concentrated in vacuum. The crude obtained was flash chromatographed using toluene: ethylacetate (95:5) to give the trans titled compound (65.0mg,0.23mmol) in 58% yield (MP: 84°C).

^1H NMR (250MHz,$CDCl_3$)δ: 2.34 (s,3H,CH_3CO), 2.91 (dd,1H, J=11.73,17.78Hz,HC$\underline{H}_a$CHC-S), 3.27 (dd,1H,J=4.10,17.77Hz,HC$\underline{H}_e$CHC-S), 3.54 (s,3H,OCH_3), 3.78 (s,3H,OCH_3), 3.82 (s,3H,OCH_3), 4.16 (dd,1H, 4.13,11.79Hz,CH-S), 5.69 (s,1H,O-CH-S), 6.75 (dd,2H,J=8.96, 14.36 Hz,ArH). IR (cm^{-1}): 2925: CH, 1705.7: C=O. Cis-3-aceto-1,5,8-trimethoxythioisochroman (32.4mg,0.11mmol) was obtained in 30% yield (MP: 129°C).

^1H NMR (250MHz,$CDCl_3$)δ: 2.34 (s,3H,CH_3), 3.25 (d,2H,J=6.58Hz, $\underline{H}_a\underline{CH}_e$CHC-S), 3.46 (s,3H,$OCH_3$), 3.59 (dd,1H,J=6.75,13.55Hz,CH-S), 3.79 (2s,6H,OCH_3), 5.73 (s,1H,O-CH-S), 6.76 (dd,2H,J=9.50,21.30Hz, ArH).

Step 3: Trans-3-aceto-1-methoxy-5,8-dioxoisothiochroman

The thioisochroman derivative from step 2 (example 13) (178.2 mg, 0.63 mmole) was dissolved in acetonitrile (10 ml) and H_2O (10 ml), followed by the addition of $NaHCO_3$ (100.8 mg, 1.22 mmole). The mixture was cooled to 0°C, followed by the slow addition of CAN (1.04g, 1.89 mmole). After 20 minutes of stirring, H_2O was added and the mixture was extracted with CH_2Cl_2. The combined organic phases were washed with H_2O, dried over $MgSO_4$, filtered and concentrated in vacuum. The crude obtained was found to be pure titled compound by ^{1}NMR and was used in the following step (>95% yield).

^1H NMR (250 MHz, $CDCl_3$)δ: 1.73 (s,3H,$COCH_3$), 2.62 (dd,1H, J=11.32, 19.81Hz,HCHaCH-S), 2.87 (dd,1H,J=4.28, 20.20Hz,HCHeCH-S), 3.21 (s, 3H,OCH_3), 3.61 (dd,1H,J=4.31, 11.42Hz,CHS), 5.97 (m,2H,HC=CH).

Step 4: Trans-3-aceto-1-methoxy-1,2,3,4-tetrahydro-(2-sulfur)anthracene-5,10-dione and cis-3-aceto-1-methoxy-1,2,3,4-tetrahydro-(2-sulfur)anthracene-5,10-dione

Trans-3-aceto-1-methoxy-5,8-dioxoisothiochroman (0.66 mmole) was dissolved in dry toluene (14ml), followed by the addition of the diene (120.0 mg, 1.07 mmole). The resulting mixture was stirred at room temperature overnight. Solvent was removed and the crude obtained was flash chromatographed using pure toluene to give the titled compounds in a ratio of about 1:1, in 48% yield.

^1H NMR (250MHz, $CDCl_3$)δ: 2.37, 2.39 (2s,6H,CH_3, cis and/or trans), 2.75 (dd,1H,J=6.42,19.81Hz,HCHaCH-S, cis or trans), 2.90 (dd,1H, J=11.79, 20.08 Hz,HCHa-CH-S, cis or trans), 3.27 (dd,1H,J=3.98, 20.0Hz,HCHeCH-S, cis or trans), 3.58 (s,3H,OCH_3, cis or trans), 3.60 (s,3H,OCH_3, cis or trans), 3.64 (m,2H,CH-S, cis or trans), 4.11 (dd,1H,J=3.92,11.80Hz,CH-S, cis or trans), 5.30 (s,1H,OCH-S, cis or trans), 5.49 (s,1H,OCH-S, cis or trans), 7.74 (m, 4H,ArH, cis and trans), 8.10 (m,4H,ArH, cis and trans). IR (cm^{-1}): 2900:CH; 1709.4:C=O; 1668.1, 1631.9:C=O quinone.

Step 5: cis-3-aceto-1-methoxy-5,8-dioxoisothiochroman

Oxidative demethylation, by using the procedure from step 3 (example 13), of cis-3-aceto-1,5,8-trimethoxythioisochroman gave the titled compound in 98% yield.

H_1 NMR (250 MHz, $CDCl_3$)δ: 2.04 (s,3H,CH_3), 2.23 (dd,1H,J=4.88, 19.49Hz, HCHaCH-S), 2.54 (d,1H,J=5.68Hz,HCHeCH-S), 3.56 (dd, 1H, J=2.10, 19.23Hz,HCHa,e-S), 5.09 (s,1H,CH-S), 5.96 (dd,2H,J=10.30, 12.20Hz,ArH).

Step 6: cis-3-aceto-1-methoxy-1,2,3,4-tetrahydro-(2-sulfur) anthracene-5,10-dione and trans-3-aceto-1-methoxy-1,2,3,4-tetrahydro-(2-sulfur) anthracene-5,10-dione

Application of the procedure described for step 4 (example 13) to trans-3-aceto-1-methoxy-5,8-dioxoisothiochroman gave pure titled compounds.

^1H NMR (250 MHz, $CDCl_3$)δ: 2.37 (s,3H,CH_3), 2.75 (dd,1H,J=6.42, 19.81Hz,HCHaCH-S), 3.58 (s,3H,OCH_3), 3.64 (m,2H,CH-S,HCHeCH-S), 5.49 (s,1H,O-CH-S), 7.74 (m,2H,ArH), 8.10 (m,2H,ArH). IR (cm_{-1}): 2900:CH; 1707.8:C=O; 1660.0, 1630.2, 1594.4:C=O quinone.

Step 7: trans-3-aceto-1-hydroxy-1,2,3,4-tetrahydro-(2-sulfur) anthracene-5,10-dione and cis-3-aceto-1-hydroxy-1,2,3,4-tetrahydro-(2-sulfur) anthracene-5,10-dione

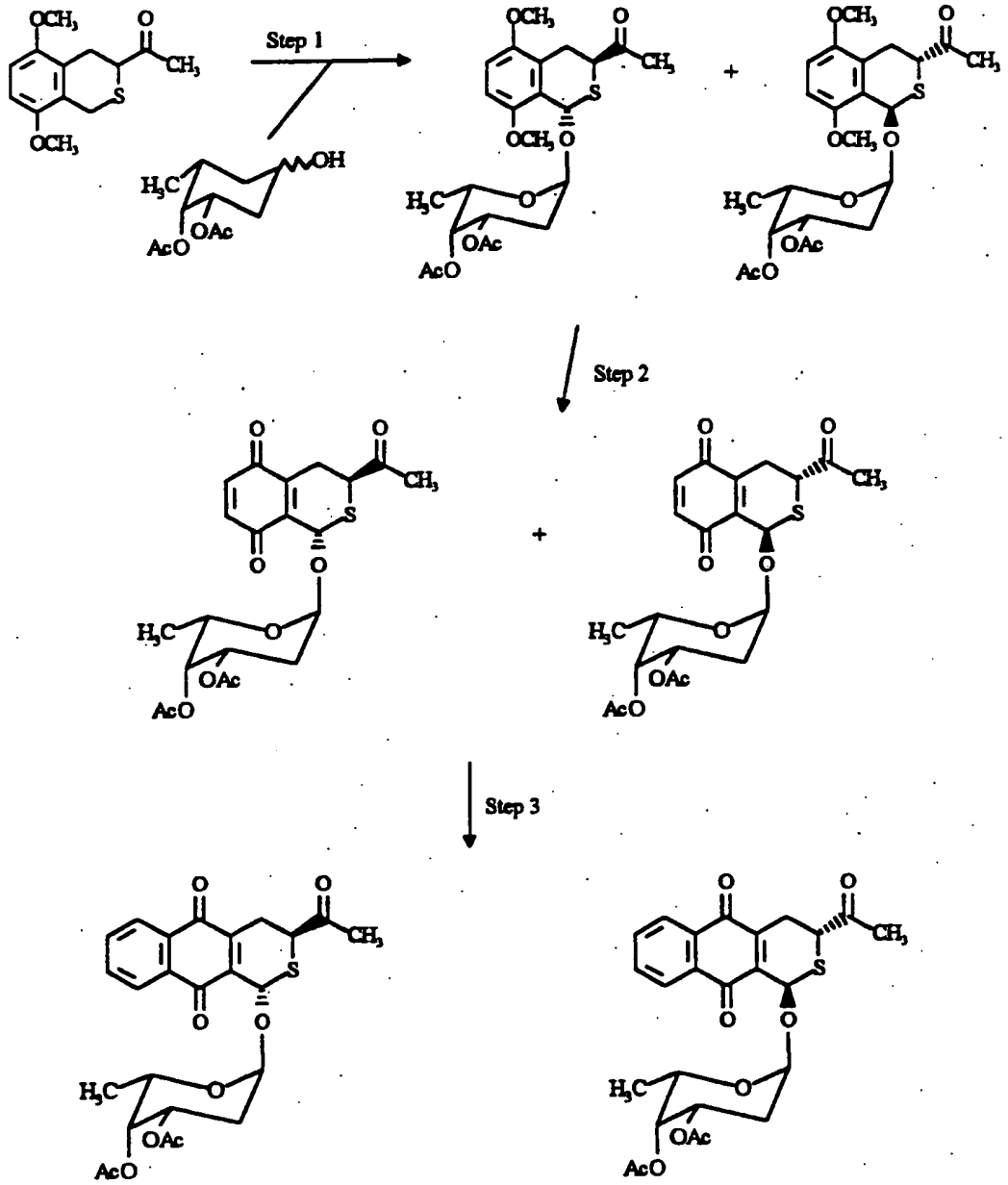
The mixture of compounds obtained from step 6 (example 13) (30.8 mg, 0.102 mmole) was dissolved in

$CH_3COOH:H_2O$ (2:0,4 ml) at 0°C. The resulting mixture was stirred at 0°C for about 2 hours. $NaHCO_3$ (5%) was added and it was extracted with CH_2Cl_2. The combined organic phases were washed with H_2O, dried over $MgSO_4$, filtered and concentrated in vacuum. The crude product obtained was flash chromatographed using hexanes:ethyl acetate (7:3) to give the titled compounds in 7% yield. According to NMR one isomer is major:

^1H NMR (250 MHz, $CDCl_3$)δ: 2.74 (s,3H,CH_3), 3.00 (dd,1H, J=11.99, 20.74Hz,HCHaCH-S), 3.26 (dd,1H,J=3.96, 20.61Hz,HCHeCH-S), 4.37 (dd, 1H,J=3.99,12.0Hz,CH-S), 6.67 (s,1H,O-CH-S), 7.73 (m,2H,ArH), 8.08 (m,2H,ArH).

EXAMPLE 14 - Thiopyranylnaphthoquinone glycosides

Example 14 Preparation of naphto[2,3-C] thiopyran glycosides.



Step 1:

(1'S,1R,3S) and (1'S,1S,3R) methyl (5,8-dimethoxy-1-(2',3',4',6'-tetradeoxy-3',4'-diacetoxy-L-lyxohexo-pyranose)-3,4,-dihydrobenzo [2,3-c] thiopyran-3-yl) ketone

A mixture of thioisochroman from step 1 (example 13) (96.0 mg, 0.38 mmol), dicyano dichloro benzoquinone (DDQ) (104.0 mg, 0.46 mmol) and 3,4-di-O-acetyl-2,6-dideoxy-L-lyxohexopyranose (_-

anomer/β-anomer=1:3; 106.4 mg, 0.46 mmol) in 5 ml of CH_2Cl_2 was stirred at room temperature under argon for 2.5 hours. After additions of 5 ml of $NaHCO_3$ solution (5%) and 10 ml of H_2O, the products were extracted with CH_2Cl_2 (25 ml x 4). The combined organic phase was washed with H_2O (15 ml), dried over $MgSO_4$, filtered and then concentrated. The residue was purified by flash chromatography (hexanes/CH_2Cl_2/ethyl acetate, 2=1=1) to provide a mixture of titled compounds (2=1, 116.9 mg, 0.24 mmol) in 64% yield along with recovered sugar (48 mg, 0.21 mmol).

^1H NMR ($CDCl_3$), the major isomersδ: 1.20 (d,3H,J=6.2Hz), 1.70-2.30 (m,2H), 1.94 (s,3H), 2.20 (s,3H), 2.29 (s,3H), 2.98 (dd,1H, J=16.5Hz,10.5Hz), 3.28 (dd,1H,J=16.5Hz,5.1Hz), 3.80 (s,6H), 4.14 (dd,1H,J=10.5Hz,5.1Hz), 4.42 (q,1H,J=6.3Hz), J6.3Hz), 5.10-5.25 (m, 2H), 5.65 (d,1H,J=3.2Hz), 6.27 (s,1H), 6.72 (d,1H,J=9.8Hz), 6.81 (d,1H,J=9.5Hz); the minor isomer: 1.19 (s,3H), 1.70-2.30 (m,2H), 1.95 (s,3H), 2.19 (s,3H), 2.34 (s,3H), 2.96 (dd,1H,J=16.5Hz, 10.5Hz), 3.30 (dd,1H,J=16.5Hz,5.1Hz), 3.81 (s,6H), 4.22 (dd,1H, J=10.5Hz,5.1Hz), 4.42 (q,1H,J=6.3Hz), 5.10-5.25 (m,2H), 5.50 (d,1H, J=3.2Hz), 6.03 (s,1H), 6.70 (d,1H,J=9.8Hz, 6.79 (d,1H,J=9.8Hz).

Step 2:

(1'S,1R,3S) and (1'S,1S,3R) methyl (5,8-dioxo-1-(2',3', 4',6'-tetradeoxy-3',4'-diacetoxy-L-lyxohexo-pyranose)-3,4,5,8-tetrahydrobenzo [2,3-c] thiopyran-3-yl) ketone

To a stirred solution of the thioisochroman glycosides from step 1 (example 14) (106.0 mg, 0.22 mmol) in 5 ml of CH_3CN was added a solution of $NaHCO_3$ (35.0 mg, 0.42 mmol) in 2 ml of water. After cooling to 0°C, a solution of CAN (362.0 mg, 0.66 mmol) in 2 ml of water was added dropwise. After being stirred at 0°C for 20 minutes, the mixture was extracted with CH_2Cl_2 (25 ml x 2). The organic layer was washed with H_2O, dried over $MgSO_4$, filtered and then concentrated. The residue (94.3 mg, 0.21 mmol) was found to be the title compounds (2:1) by ^1H NMR. The yield was 95%.

^1H NMR ($CDCl_3$), the major isomer: δ: 1.28 (d,3H,J=7.6Hz), 1.53-2.40 (m,2H), 1.99 (s,3H), 2.17 (s,3H), 2.33 (s,3H), 2.74 (dd,1H,J=18.8Hz,11.0Hz), 3.14 (dd,1H,J=18.8Hz,4.8Hz), 4.00 (dd,1H,J=11.0Hz,4.8Hz), 4.24 (q,1H,J=7.6Hz), 4.95-5.20 (m,2H), 5.56Hz (d,1H,J=3.2Hz), 6.00 (s,1H), 6.19 (d,1H,J=11.0Hz), 6.85 (d,1H,J=11.0Hz); the minor isomer: 1.18 (d,3H,J=7.5Hz), 1.53-2.40 (m,2H), 1.99 (s,3H), 2.17 (s,3H), 2.37 (s,3H), 2.70 (dd,1H,J=19.0Hz,10.5Hz) 3.15 (dd,1H,J=19.0Hz,4.8Hz), 4.07 (dd,1H,J=10.5Hz,4.8Hz), 4.33 (q,1H,J=7.5Hz), 4.95-5.20 (m,2H), 5.52 (d,1H,J=3.2Hz), 5.77 (s,1H), 6.70 (d,1H,J=11.0Hz), 6.78 (d,1H,J=11.0Hz).

Step 3:

(1'S,1R,3S) and (1'S,1S,3R) methyl (5,8-dioxo-1-(2',3', 4',6'-tetradeoxy-3',4'-diacetoxy-L-lyxohexopyranose)-3,4,5,10-tetrahydronaphtho [2,3-c] thiopyran-3-yl) ketone

The procedure for the preparation of the titled compound is as described previously in step 1 (example 1).

Thus, the reaction of the isochromandiones (94.3 mg, 0.21 mmol), obtained from the previous step with 1-acetoxy butadiene (0.10 ml, 94.5 mg, 0.84 mmol) gave the titled compounds 2:1 (74.2 mg, 0.15 mmol) in 70% yield after flash chromatography.

^{1}H NMR ($CDCl_3$), the major isomer had δ: 1.32 (d,3H,J=6.5Hz), 1.70-2.40 (m,2H), 1.94 (s,3H), 2.17 (s,3H), 2.36 (s,3H), 2.91 (dd,1H, J=20.0Hz,11.9Hz), 3.30 (dd,1H,J=19.9Hz,4.2Hz), 4.06 (dd,1H, J=12.0Hz,4.1Hz), 4.38 (m,1H), 5.05-5.22 (m,2H), 5.61 (d,1H, J=3.8Hz), 6.23 (s,1H), 7.70-7.80 (m,2H), 8.05-8.15 (m,2H); the minor isomer had δ: 1.19 (d,3H,J=6.5Hz), 1.70-2.40 (m,2H), 1.95 (s,3H), 2.17 (s,3H), 2.39 (s,3H), 2.87 (dd,1H,J=20.0Hz,12.0Hz), 3.32 (dd,1H,J=20.0Hz,4.1Hz), 4.15 (dd,1H,J=12.0Hz,4.1Hz), 4.38 (m, 1H), 5.05-5.22 (m,2H), 5.63 (d,1H,J=3.8Hz), 6.00 (s,1H), 7.70-7.80 (m,2H), 8.05-8.15 (m,2H), IR (neat): 3866, 2987-2939, 1745(s), 1715, 1667, 1645, 1597, 1368, 1285, 1252, 1229, 1021, 988, 737 cm_{-1}.

EXAMPLE 15 - In Vitro Cytotoxicity - Microculture Tetrazolium Assay

The microculture tetrazolium assay was used to test in vitro cytotoxicity. This assay is described in Plumb, J.A. et al., 1989 Cancer Research 49, 4435-4440, which is herein incorporated by reference. The cytotoxicity of compounds towards tumor cells is measured in vitro using the assay. This assay method is based upon the ability of live, but not dead cells to reduce the yellow water soluble dye 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) to its water insoluble purple formazan product.

The following reagents were used for :

tissue Culture, (Irvine Scientific Catalog)

-MEM containing nucleosides (Catalog # 9144)

Fetal Bovine Serum (Catalog # 3000)

Non-essential amino acids (Catalog # 9304)

Dulbecco's phosphate buffered saline (Catalog # 9240)

Sodium pyruvate (Catalog # 9334).

All other tissue culture and general reagents were from Sigma Chemical Company.

Human Tumor Cell lines, used were:

SKOV3 (Ovarian adenocarcinoma) - provided by Dr. V. Ling, Ontario Cancer Institute.

SKVLB (Ovarian; multidrug resistant) - Dr. V. Ling, Ontario Cancer Institute.

T47D (Ductal carcinoma of breast) - ATCC catalog # HTB-133.

Lox (Melanoma) - Southern Research Institute.

HT 29 (Colon adenocarcinoma) ATCC catalog # HTB-38.

The cells were maintained in exponential growth in culture in minimal essential media (MEM) supplemented with non-essential amino acids, and containing 15% (v/v) fetal bovine serum, 5mM L-glutamine, 1 mM sodium pyruvate, and 0.1 U/ml insulin. All cell lines were grown at 37°C in an atmosphere of 5% CO_2 in air.

Stock solutions, used were the following;

MTT:	2 mg/ml in phosphate buffered saline (stable at 4°C in dark for 1 week).
Sorensen's buffer:	0.1M glycine/NaOH, pH 10.5, containing 0.1M NaCl.
Test compounds:	20 mM in DMSO and diluted to a final concentration of 200 μM in culture medium before use.

The following is the generic description of the assay method. It should be noted that although the conditions described work well with the cells listed above, the initial plating density and the MTT concentration used should be verified for each new cell line used to test compounds.

For each assay, doxorubicin is included as an inter-assay standard. This allows us to monitor the behaviour of the assay in general, and in particular, to check that the SKVLB line has maintained its resistant phenotype.

The plate layout is done in the following manner:
The assays are carried out in 96-well (8 well x 12 well) microtiter plates. Serial dilutions of the compound are tested along the length of the plate. A 1:3 serial dilution of compound in culture medium covers a concentration range from 100 μM to 1.7nM. Each concentration of compound is tested in quadruplet, allowing two compounds to be tested per plate. Wells containing no cells (blank) and cells with no test compound (control) are included on each plate.

Cells are plated out in 100 μl of culture medium in the microtiter plates at a density of around 1,500 - 4,000 cells per well. The plates are incubated overnight to allow the cells to become adherent after which the test compound is added (100 μl of appropriate dilution per well). The cells are incubated with test compound at 37°C for 48h after which the compound is replaced with fresh medium. After a further 48h incubation at 37°C, 50 μl of MTT solution (2mg/ml) is added to each well. The plates are incubated in the dark for 4h at 37°C after which the medium is removed. The MTT formazan product is extracted from the cells by the addition of 200 μl DMSO followed by 50 μl of Sorensen's buffer. The plates are shaken briefly and the absorbance at 570 nm is read using a Molecular Devices UV max plate reader. Curves are fit to the MTT assay data using a four parameter logistic equation, and the data are normalized to fit a 0% to 100% survival scale.

RESULTS

Tables 1 and 2 show the antitumor activity of some of synthetic tricyclic pyranylnaphthoquinones of this invention. A range of potency is observed. In this set of compounds. Several tricyclic naphthoquinones are intensely potent and are effective in the multidrug resistant cell line SKVLB. In breast cancer, MCF-7, BCH-1146 is less potent than adriamycin but nearly as effective in the sensitive and adriamycin resistant cell line. These results suggest that tricyclic derivatives such as BCH-1184 and 1146 should be

useful in the treatment of certain resistant cancers. Most notably BCH-2051, a "sugarless" tricyclic naphthoquinone, possesses intense in vitro antitumor potency while significantly avoiding multidrug resistance as observed from the SKVLB cell line.

EXAMPLE 15

BIOLOGICAL RESULTS

TABLE 1

IC_{50} µM

COMPOUND	SKOV3	SKVLB	T47D	LOX	HT29	VLB/OV3
Adriamycin	0.012	1.49	0.07	0.034	0.090	121.5
BCH1125	>100	92.90	36.40	52.80	>100	
BCH1129	73.30	>100	59.40	88.20	63.20	
BCH1146	0.8910	6.97	5.87	3.82	0.9100	7.82
BCH1148	>100	>100	>100	>100	>100	
BCH1169	7.14	60.10	26.50	9.63	6.29	8.42
BCH1177	9.67	16.50	13.30	29.70	25.10	1.71
BCH1180	0.8510	8.68	7.61	3.33	0.4680	10.20
BCH1181	2.26	8.48	9.23	3.07	0.5360	3.75
BCH1184	0.0050 - -0.0631	0.0536 - 0.3000	0.2840 - 0.5300	0.0186 - -0.2280	0.0023 - 0.0161	4.75 - 22.34
BCH1188	0.8590	2.41	0.6640	0.9470	2.49	2.81
BCH1189	6.50	26.60	12.50	14.30	16.60	4.09
BCH1192	28.60		31.60	29.90	37.60	
BCH1607	7.26	19.80	14.70	8.97	21.60	2.73
BCH1608	3.31	15.10	9.55	5.22	14.30	4.56
BCH1620	0.0042	0.2160	0.1830	0.0227	0.0328	51.31
BCH1643	1.74	5.17	3.49	1.65	6.71	2.97
BCH1644	0.5050	1.52	1.27	0.6410	2.65	3.01
BCH1648	0.0519	0.3150	0.3600	0.1380	0.3090	6.07
BCH1649	0.1100	0.4590	0.3800	0.2170	0.3310	4.17
BCH1654	0.7100	3.73	1.59	1.19	3.58	5.25
BCH1658	0.2330	1.47	0.4940	0.3160	0.6610	6.31
BCH1665	25.40	28.90		11.50	60.40	1.14
BCH1666	0.2720	0.2050		0.1250	0.0783	0.75
BCH1667	0.0122	0.0893		0.0133	0.0016	7.32
BCH1688	0.6340	2.77		0.4020	1.35	4.37
BCH1689	2.78	16.50		1.72	3.66	5.94
BCH1690	1.78	13.70		1.62	3.01	7.70

BCH1691	8.83	18.50		4.49	7.16	2.10
BCH1693						
BCH1697	3.70	13.20	18.00	5.32	11.00	3.57
BCH1998	0.1250	1.66	0.1140	0.0631	0.0363	13.28
BCH2000	0.0950	6.64	0.3380	0.0905	0.0378	69.89
BCH2014	21.50	39.80	61.80	35.90	61.30	1.85
BCH2015	0.3670	1.17	0.9090	1.09	0.5570	3.19
BCH2017	0.2500	8.94	0.4970	0.2500	0.4300	35.76
BCH2018	3.11	17.70	8.56	2.38	14.20	5.69
BCH2019	0.0633	0.3280	0.0486	0.0627	0.0230	4.95
BCH2020	11.20	25.90	9.42	5.45	19.10	2.31
BCH2021	12.40	46.40	19.00	10.60	37.80	3.74
BCH2022	0.4420	1.87	0.9340	0.4840	0.5320	4.23
BCH2023	0.73	3.2	5.5	0.67	0.98	4.39
BCH2024	0.924	5.23	3.7	0.85	0.404	5.66
BCH2026	15	>100	31.40	2.12	22	>7
BCH2027	7.01	29	23.30	3.04	15.40	4.02
BCH2031	6.0	18	16	2.8	8.5	3
BCH2032	6.01 - 12	17.60 - 28	15.80 - 23	2.83 - 5.1	8.49 - 9.3	2 - 2.93
BCH2035	0.28	6.23	1.5	0.75	2.31	22.33
BCH2037	0.59 - 5.09	3.8 - 4.73	2.2 - 2.29	0.54 - 0.816	1.1 - 4.25	0.93 - 6.41
BCH2038	0.832	3.5	2.0	0.173	2.0	4.16
BCH2041	2.14	10	5.62	1.9	1.9	5
BCH2042	3.8	13.20	8.0	2.22	1.2	3.51
BCH2043	3.1	9.23	11	2.92	4.7	3
BCH2044	1.44	5.11	4.25	0.38	0.194	3.55
BCH2045	5.3	15	13	4.6	1.11	3
BCH2046	0.0075	0.22	0.0675	0.015	0.0071	31
BCH2047	0.017	0.523	0.151	0.021	0.0041	31
BCH2051	0.0073 -0.029	0.0675 - 0.403	0.0419 - 0.0685	0.0167 - 0.03	0.091 - 0.134	9.3 - 14.14
BCH2052	5.4 - 7.01	20.50 - 28.20	9.54 - 23.30	3.04 - 3.22	10.60 - 15.40	3.78 - 4.02
BCH2053	4.73	21.20	12.30	3.25	14	4.48
BCH2054	6.33	11.30	4.95	3.23	4.30	1.79

BCH2060	1.14	2.5	0.562	1.95	0.26	2.19
BCH2061	0.0083	0.141	0.27	0.045	0.054	18
BCH2062	0.8100	0.8420	0.7760	0.3540	1.14	1.04
BCH2065	1.54	6.1	2.2	1.4	3.42	4
BCH2067	1.2	2.24	0.54	1.1	0.323	2
BCH2068	1.2	1.2	0.422	1.3	0.13	1
BCH2069	0.0494	0.083 - 0.483	1.11	0.0903	0.35	2 - 9.78
BCH2070	0.0084	0.12	0.018	0.015	0.006 - 0.534	14.34 - 15
BCH2071	0.133	0.43	0.201	0.21	0.05	3.22
BCH2072	0.0641 - 0.1130	0.315 - 0.991	0.0236 -0.35	0.102	0.0539 -0.101	2.79 - 15.46
BCH2075	16	31	13	8.8	31	2
BCH2076	1.43	12.40	6.53	1.8	2.6	9
BCH2077	1.94	21	7.7	1.91	3.4	11
BCH2078	0.4140	2.24	0.5070		0.2690	5.41
BCH2079	0.0163	0.124	0.032	0.066	0.005	8
BCH2081	1.3	19	7.4	2.7	3.8	15
BCH2082	1.8	5.6	4.0	1.6	2.6	3
BCH2087	0.069	0.472	0.18	0.064	0.028	7
BCH2090	11	36			10.40	3.29
BCH2091	13.40	32	16	3.3	11.30	3
BCH2092	1.1	3.0	0.98	0.30	2.42	3
BCH2095	0.19	1.6	0.37	0.14	0.0996	8.16
BCH2096	0.702	3.11	1.7	0.84	1.7	4.43
BCH2098	8.0	30	10	4.2	17	4
BCH2099	0.599 - 2.0	0.462 - 8.4	0.728 - 3.4	0.128 - 1.1	0.303 - 1.7	0.77 - 2
BCH2100	2.7	8.22	4.0	3.0	5.12	3.04
BCH2101						
BCH2102	0.13	0.723	0.30	0.186	0.15	5.65
BCH2104	0.21	1.1	0.613	0.24	0.171	5.05
BCH2105	0.003	0.37	0.019	0.025	0.0069	123
BCH2109	0.79	3.2	1.04	1.1	0.12	4.02
BCH2112	0.104	1.7	0.27	0.21	0.065	15.96 - 17

BCH2113	0.171	0.72	0.27	0.19	0.059	4.20
BCH2114	0.4720	2.04	0.6550	0.3730	0.2570	4.32
BCH2115	2.3	>100	5.3	4.0	5.6	>50
BCH2117	0.0095	0.332	0.0374	0.073	0.03	35.13
BCH2118	0.12	0.79	0.244		0.203	6.68
BCH2119	>100	>100	>100		>100	
BCH2121	0.21	1.3		0.34	.34	
BCH2122	0.37	2.0		0.73	0.64	
BCH2123						
BCH2124						
BCH2126	0.6770	1.68	0.7060	0.3730	3.95	2.48
BCH2127	0.35	4.1		2.0	2.7	
BCH2128	1.7	5.8		1.4	1.6	
BCH2129	0.3590	1.06	0.4520	0.2280	2.07	2.95
BCH2131	35.80	34.60	12.80	12.50	43.40	0.97
BCH2132	99.80	70.60	34.70	28.40	>100	0.71
BCH2135	0.66	1.3	1.1	0.31		0.88
BCH2138	>100	>100	90	>100		>100
BCH2140	2.2	13	1.5	0.45		3.2
BCH2141	8.12	9.96	3.79	1.82	6.44	1.23
BCH2142	92	46	45	18		>100
BCH2143						
BCH2144	21.40	16.10	7.22	3.28	5.93	0.75
BCH2145	8.19	13.40	1.78	0.8300	2.48	1.64
BCH2147	12.50	10.10	3.92	1.88	10.00	.081
BCH2148	12.60	9.93	2.36	1.55	7.50	0.79
BCH2149	32.70	29.80	11.40	10.00	28.20	0.91
BCH2150						
BCH2151						
BCH2152						
BCH2153						
BCH2154						
BCH2155						
BCH2157						
BCH2158						
BCH2159						
BCH2160						
BCH2161						
BCH2162						

BCH2163

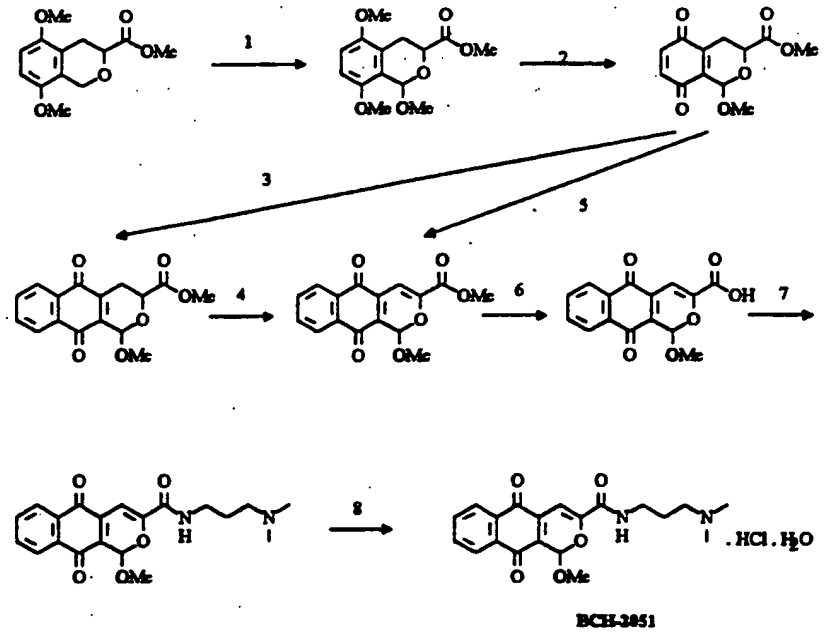
BCH2164

TABLE 2

IC_{50} μM

COMPOUND	MCF-7	MCF-7/ADR	MAT-B	MAT-B/ADR
Adriamycin	0.005	6.5	0.0046	2.50
1146	0.044	0.19	0.46	0.56
1177	>10.0	0.66	>10.0	>10.0

Example 16: Preparation of naphthopyran derivatives



BCH-3851

Step 1: Methyl (1,5,8-trimethoxyisochroman-3-yl) formate

Methyl (5,8-dimethoxy-isochroman-3-yl) formate (15.00 g, 59.46 mmol) and DDQ (16.20 g, 71.35 mmol) were dissolved in dry dichloromethane (500 ml), and dry methanol (7.2 ml, 178.37 mmol) was added. The solution was stirred at ambient temperature overnight, then refluxed for 8 hours. Methanol (1.0 ml, 24.69 mmol) and DDQ (2.00 g, 8.81 mmol) was added and further refluxed for 8 hours. The reaction mixture was cooled down, filtered, and the filtrate was poured onto a saturated solution of sodium bicarbonate (200 ml). The organic phase was separated, washed with saturated sodium bicarbonate solution (100 ml), dried ($MgSO_4$) and evaporated under reduced pressure. The residue was recrystallized from methanol to give the title product (white crystals, 14.34 g, 85.1 %).

^{1}H-NMR (250 MHz, Brucker, $CDCl_3$), d: 2.70 (1H, dd, J=11.8 and 17.1 Hz, 4-H_{ax}), 3.08 (1H, dd, J=4.2 and 17.1 Hz, 4-H_{eq}), 3.57 (3H, s, 1-MeO), 3.77 (3H, s, Ar-OMe), 3.80 (3H, s, Ar-OMe), 3.83 (3H, s, COOMe), 4.79 (1H, dd, J=4.2 and 11.8 Hz, 3-H_{ax}), 5.70 (1H, s, 1-H), 6.68 (1H, d, J=8 Hz, Ar-H), 6.74 (2H, d, J=8 Hz, Ar-H).

Step 2: Methyl (1-Methoxy-5,8-dioxo-5,8-dihydro-isochroman-3-yl) formate

The solution of CAN (83.24 g, 151.84 mmol) and sodium bicarbonate (8.50 g, 101.22 mmol) in water (500 ml) was added to the solution of methyl (1,5,8-trimethoxy-isochroman-3-yl) formate (14.34 g, 50.61 mmol) in acetonitrile (700 ml) at 0 - 5 C° over 20 minutes. The reaction mixture was stirred at 0 C° for 20 minutes, then extracted with dichloromethane (4x200 ml). The combined organic phases were

washed with brine (200 ml), dried ($MgSO_4$) and evaporated under reduced pressure to give a light yellow solid (12.76 g, quantitative yield) which was used for the next step without further purification.
^{1}H-NMR (250 MHz, Brucker, $CDCl_3$), d: 2.52 (1H, dd, J=11.4 and 19.4 Hz, 4-H_{ax}), 2.83 (1H, dd, J=4.2 and 19.4, 4-H_{eq}), 3.56 (1H, s, 1-MeO), 3.82 (1H, s, COOMe), 4.66 (1H, dd, J=4.2 and 11.4 Hz, 3-H_{ax}), 5.48 (1H, s, 1-H), 6.62 (1H, d, CHCO), 6.78 (1H, d, CHCO).

Step 3: **Methyl (1-methoxy-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho[2,3-c]pyran-3-yl) formate**

Methyl (1-methoxy-5,8-dioxo-5,8-dihydro-isochroman-3-yl) formate (12.70 g, 50.35 mmol), 1-acetoxybutadiene (30.00 g, 267.55 mmol) and dry toluene (100 ml) was stirred overnight at 50 C°. The solvent was removed under reduced pressure, the residue was recrystallized from methanol to give yellow crystals (11.05 g). The product was dissolved in toluene (200 ml), silica gel (20 g) was added and stirred over 24 hours in an open flask at ambient temperature. The silica was filtered, the filtrate was concentrated to dryness. The residue was recrystallized in methanol. The mother liquor was concentrated to dryness and the silica gel treatment was repeated as above. After recrystallization the mother liquor was concentrated to dryness and the residue was purified by flash chromatography on silica. Eluent: toluene/ethyl acetate (4/1). All the crystals and the clean fraction from flash chromatography were combined to give 9.07 g, (59.6 %) title product.
^{1}H-NMR (250 MHz, Brucker, $CDCl_3$), d: 2.68 (1H, dd, J=11.1 and 19.9 Hz, 4-H_{ax}), 3.07 (1H, dd, J=4.4 and 19.9 Hz, 4-H_{eq}), 3.62 (1H, s, 1-MeO), 3.83 (1H, s, COOMe), 4.72 (1H, dd, J=4.4 and 11.1 Hz, 3-H_{ax}), 5.70 (1H, s, 1-H), 7.75 (2H, m, Ar-H), 8.08 (2H, m Ar-H).

Step 4: **Methyl (1-methoxy-5,10-dioxo-5,10-dihydro-1H-naphtho[2,3-c]pyran-3-yl) formate**

Methyl (1-methoxy-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho[2,3-c]pyran-3-yl) formate (6.12 g, 20.25 mmol) was dissolved in dichloromethane (120 ml), triethylamine (5.64 ml, 40.49 mmol) was added and stirred at ambient temperature over 1 hour. The reaction mixture was poured onto water (100 ml) and ethyl acetate(400 ml), then neutralized with acetic acid. The organic layer was separated, the water layer was extracted with ethyl acetate (3x30 ml). The combined organic layers were dried ($MgSO_4$) and concentrated to dryness. To the residue dichlorometane (60 ml) and saturated sodium bicarbonate solution (20 ml) was added, then stirred for 5 minutes. After separation the organic layer was dried ($MgSO_4$) and concentrated to 10 ml. This solution was filtered through a short silica gel column. Eluent: dichloromethane and 5% ethyl acetate in dichloro-methane. The clean fractions were combined and concentrated to dryness to give the title product (5.49g, 90.3 %).
^{1}H-NMR (250 MHz, Brucker, $CDCl_3$), d: 3.63 (3H, s, 1-MeO), 3.92 (3H, s, COOMe), 6.38 (1H, s, 1-H), 7.33 (1-H, s, 4-H), 7.75 (2H, m, Ar-H), 8.13 (2H, m, Ar-H).

Step 5: **Methyl (1-methoxy-5,10-dioxo-5,10-dihydro-1H-naphtho[2,3-c]pyran-3-yl)formate.**

Methyl (1-methoxy-5,8-dioxo-5,8-dihydro-isochroman-3-yl) formate (12.70 g, 50.35 mmol), 1-acetoxybutadiene (30.00 g, 267.55 mmol) and dry toluene (100 ml) was stirred overnight at 50 C°. The solvent was removed under reduced pressure, the residue was recrystallized from methanol to give yellow crystals (11.05 g). The product was dissolved in dichloromethane (200 ml), triethylamine (10.2 ml, 73.11 mmol) was added and stirred at ambient temperature over 1 hour. The reaction mixture was poured onto water (200 ml) and ethyl acetate(800 ml), then neutralized with acetic acid. The organic layer was separated, the water layer was extracted with ethyl acetate (3x30 ml). The combined organic layers were dried ($MgSO_4$) and concentrated to dryness. To the residue dichlorometane(120 ml) and saturated sodium bicarbonate solution (40 ml) was added, stirred for 5 minutes. After separation the organic layer was dried ($MgSO_4$) and concentrated to dryness to give the title product (8.98 g, 59.4 %).
^{1}H-NMR (250 MHz, Brucker, $CDCl_3$), d: 3.63 (3H, s, 1-MeO), 3.92 (3H, S, COOMe), 6.38 (1H, s, 1-H), 7.33 (1-H, s, 4-H), 7.75 (2H, m, Ar-H), 8.13 (2H, m, Ar-H).

Step 6: 1-Methoxy-5,10-dioxo-5,10-dihydro-1H-naphtho[2,3-c]pyran-3-carboxylic acid

Methyl (1-methoxy-5,10-dioxo-5,10-dihydro-1H-naphtho[2,3-c]pyran-3-yl) formate (6.31 g, 21.01 mmol) was suspended in tetrahydrofuran (126 ml) and sodium hydroxide (0.92 g, 23.12 mmol) dissolved in water (63 ml) was added dropwise at 0 C° over 30 minutes. The reaction mixture was stirred at 0 C° over 1 hour, then it was acidified to pH = 3 with 5% hydrochloric acid. Sodium chloride (2 g) was added. The water layer was separated and extracted with ethyl acetate (3x40 ml). The water layer was acidified to pH = 2. The crystals formed were filtered and washed with water. The filtrate was extracted with ethyl acetate (4x40 ml). All the organic fractions - including the previous extractions as well - were combined, dried ($MgSO_4$) and concentrated to dryness. The residue was combined with the crystals filtered out of the water phase before, and stirred with methanol (50 ml). for 15 minutes. The yellow crystals were filtered, washed with methanol to give the title product (5.21 g, 86.6 %).
^{1}H-NMR (250 MHz, Brucker, DMSO-d_6), d: 3.50 (3H, s, 1-MeO), 6.37 (1H, s, 1-H), 7.02 (1H, s, 4-H), 7.90 (2H, m, Ar-H), 8.05 (2H, m, Ar-H).

Step 7: 1-Methoxy-5,10-dioxo-5,10-dihydro-1H-naphtho[2,3-c]pyran-3-[N-(3-dimethylamino-propyl)carboxamide]

1-Methoxy-5,10-dioxo-5,10-dihydro-1H-naphtho[2,3-c]pyran-3-carboxylic acid (4.6 g, 16.13 mmol) was suspended in tetrahydrofuran (46 ml) and DMF (0.1 ml) was added. The suspension was cooled to 0 C° and oxalyl chloride (3.24 ml, 37.09 mmol) was added dropwise over 10 minutes. The reaction mixture was stirred at 0 C° over 30 minutes, then evaporated to dryness at reduced pressure. The residue was dissolved in tetrahydrofuran (50 ml), cooled to 0 C° and N,N-dimethylaminopropylamine (2.23 ml, 17.74 mmol) was added dropwise over 10 minutes. The solution was stirred at 0 C° over 15 minutes, then it was poured onto a saturated solution of potassium carbonate (20 ml). The organic layer was separated, the water layer was extracted with dichloromethane (3x10 ml). The combined organic phases

were dried ($MgSO_4$) and concentrated to dryness. The residue was dissolved in methanol (50 ml) and stirred with charcoal at ambient temperature over 30 minutes. After filtration the filtrate was concentrated to dryness. The residue was dissolved in a minimal amount of methanol and ether (15 ml) was added. The crystals were filtered, washed with ether to give the title product (4.15 g, 69.6 %).

^{1}H-NMR (250 MHz, Brucker, $CDCl_3$), d: 1.74 (2H, quint., CH_2), 2.29 (6H, s, NMe_2), 2.47 (2H, m, CH_2), 3.35 - 3.65 (2H, m, CH_2), 3.63 (3H, s, 1-MeO), 6.37 (1H, s, 1-H), 7.33 (1H, s, 4-H), 7.75 (2H, m, Ar-H), 8.15 (2H, m, Ar-H), 8.70 (1H, broad, NH).

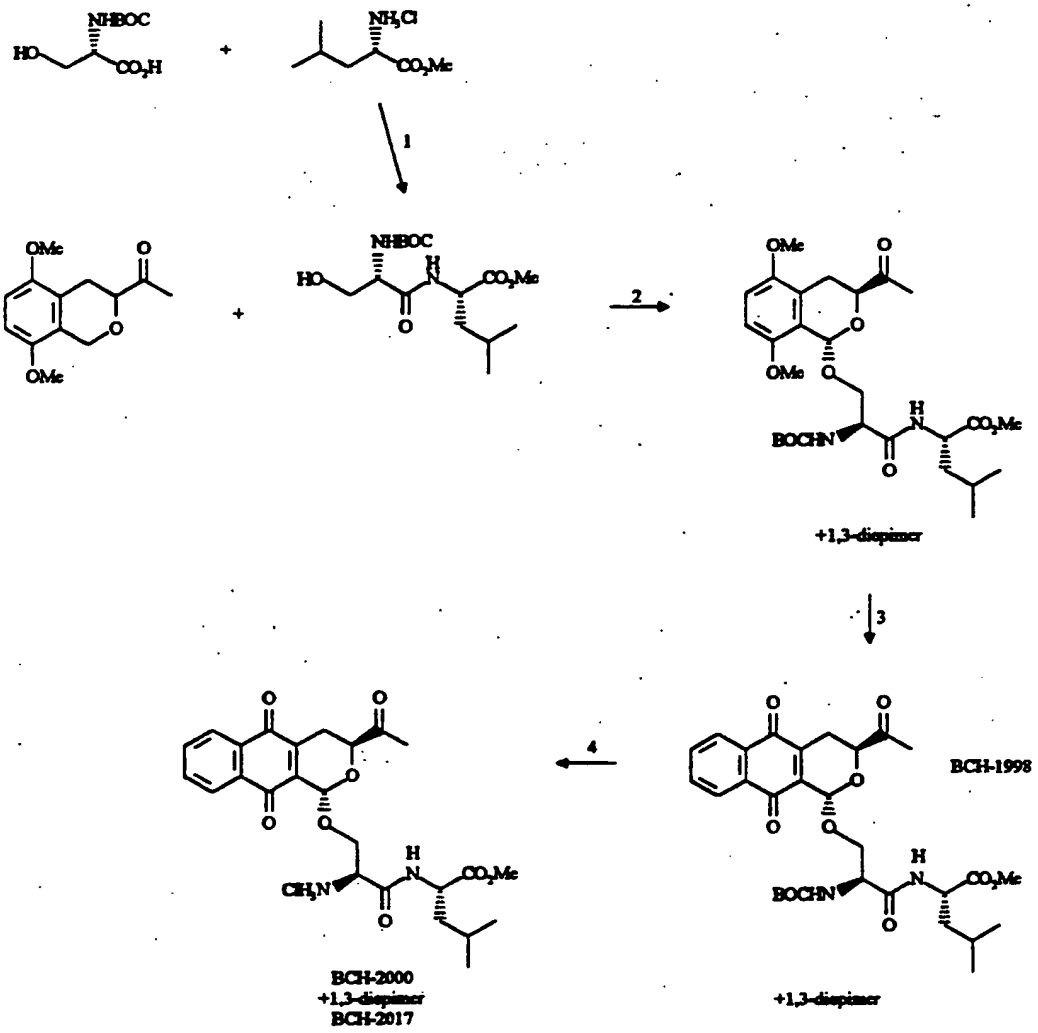
Step 8: 1-Methoxy-5,10-dioxo-5,10-dihydro-1H-naphtho[2,3-c]pyran-3-[N-(3-dimethylamino-propyl)carboxamide] hydrochloride monohydrate BCH-2051

1-Methoxy-5,10-dioxo-5,10-dihydro-1H-naphtho[2,3-c]pyran-3-[N-(3-dimethylamino-propyl)carboxamide] (4.15 g, 11.23 mmol) was dissolved in anhydrous dichloromethane (10 ml) and 1 M hydrochloric acid solution in ether (11.3 ml, 11.23 mmol) was added dropwise at 0 C°. At the end more ether (20 ml) was added and the suspension was stirred at 0 C° over 30 minutes. The crystals were filtered under argon atmosphere, washed with dry ether and hexane to give the title product (4.32 g, 90.5 %).

^{1}H-NMR (250 MHz, Brucker, DMSO-d_6), d: 1.90 (2H, m, 2'-CH_2), 2.72 (6H, s, NMe_2), 3.00 (2H, m, 3'-CH_2), 3.30 (2H, m, 1'-CH_2), 3.60 (3H, s,MeO), 6.35 (1H, s, 1-H), 7.00 (1H, s, 4-H), 7.90 (2H, m, Ar-H), 8.05 (2H, m, Ar-H), 8.92 (1H, t, CONH), 10.53 (1H, broad, NH^+).

^{13}C-NMR (250 MHz, Brucker, DMSO-d_6), d: 23.8, 36.1, 41.8, 54.0, 56.2, 94.9, 98.1, 124.5, 125.6, 126.1, 130.9, 131.5, 134.1, 134.5, 149.9, 159.6, 181.2, 181.4.

Example 17: Dipeptide substituted naphthoquinone derivative



Step 1: **N-BOC-Serine-Leucine-OMe**

To a solution of Leucine-Me ester.HCl (0.91 eq, 0.40 g) and triethylamine (1.2 eq, 0.3 ml) in dry chloroform (24 ml), under argon, at room temperature, was added N-Boc-Serine (0.50 g, 2.43 mmols) and then EEDQ (1.3 eq, 0.71 g). The solution was stirred for 18 hours after which the solvent was evaporated. The residue was taken up in EtOAc and washed with 5% HCl (2x), sat. aq. $NaHCO_3$ and brine. The organic phase was dried over Na_2SO_4, the solids filtered and the solvant evaporated to give 0.71 g (87%) of N-Boc-Ser-Leu-OMe as a clear oil that was used without further purification.
^1H NMR ($CDCl_3$): δ 7.30 (bs, 1H, NH), 5.72 (bs, 1H, NH), 4.51 (m, 1H), 4.19 (m, 1H), 3.90 (m, 1H), 3.68 (s, 3H), 3.62 (m, 2H), 1.55 (m, 3H), 1.34 (s, 9H), 0.79 (m, 6H).

Step 2: **(1S,2'S,3R,5'S) and (1R,2'S,3S,5'S)-1-[O-N-BOC-Serine-Leucine-Me ester]-3-aceto-5,8-dimethoxy-isochroman**

To a solution of 5,8-dimethoxy-3-aceto-isochroman (0.46g, 1.93 mmole), the peptide from step 1 (example 17) (0.71 g, 1.1 eq) and activated 4A molecular sieves (500 mg) in dry CH_2Cl_2 (19 ml) was added DDQ (0.57 g, 1.3 eq). The solution was stirred for 18 hours after which it was filtered through celite. It was then poured in sat. aq. $NaHCO_3$ and the phases were separated. The aqueous phase was extracted with CH_2Cl_2 (2x) and the combined organic extracts were dried over $MgSO_4$. The solids were filtered and the solvent was evaporated to give the titled mixture of diastereomers that were separated by chromatography (silica gel, 1:1 hexanes/EtOAc).

The first running fraction: 0.395 g (36%). ^{1}H NMR ($CDCl_3$): δ 7.00 (bs, 1H, NH), 6.74 (d, 1H, J = 9.0, ArH), 6.68 (d, 1H, J = 9.0, ArH), 5.81 (s, 1H, H-1), 5.64 (bs, 1H, NH), 4.52 (m, 2H), 4.29 (m, 1H), 4.05 (m, 1H), 3.88 (dd, 1H, J = 7.4, 10.6), 3.81 (s, 3H, ArOMe), 3.73 (s, 3H, ArOMe), 3.57 (s, 3H, CO_2Me), 3.00 (dd, 1H, J = 4.1, 17.6, H-4), 2.47 (dd, 1H, J = 12.3, 17.6, H-4), 2.29 (s, 3H, COMe), 1.57-1.46 (m, 3H, CH_2-CH(Me)$_2$), 1.41 (s, 9H, t-Bu), 0,84 (d, 3H, J = 3.3, isopropyl), 0.82 (d, 3H, J = 3.3, isopropyl).

The second running fraction: 0.420 g (38%), ^{1}H NMR ($CDCl_3$): δ 6.79 (m, 3H, 2ArH+NH), 6.10 (bs, 1H, NH), 5.74 (s, 1H, H-1), (4.62-4.33 (m, 3H), 3.91 (m, 2H), 3.77 (s, 6H, 2 ArOMe), 3.68 (s, 3H, CO_2Me), 3.01 (dd, 1H, J = 4.0, 17.6, H-4), 2.50 (dd, 1H, J = 12.3, 17.6, H-4), 2.33 (s, 3H, COMe), 1.50 (s, 9H, t-Bu), 1.48-1.25 (m, 3H, CH_2-CH(Me)$_2$), 0.70 (d, 3H, J = 5.7, isopropyl), 0.61 (d, 3H, J = 5.7, isopropyl).

Step 3: (1S,2'S,3S,5'S)-Methyl-(1-O-[N-BOC-Serine-Leucine-Me ester]-5,10-dioxo-3,4,5,10-tetrahydro-1-H-naphtho [2,3-c] pyran-3-yl) ketone

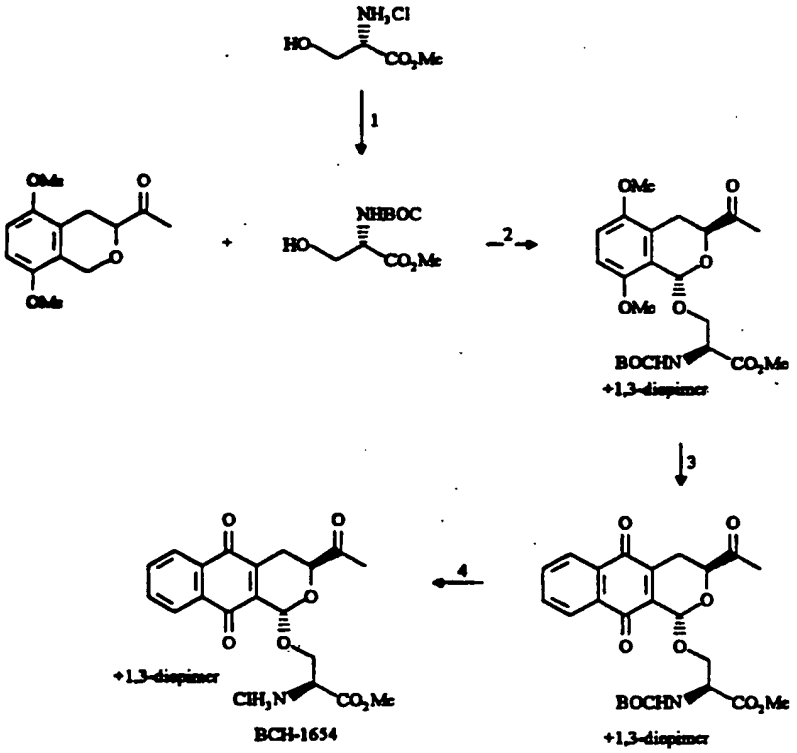
To a solution of the peptido-isochroman from step 2 (example 17) (0.40 g, 0.68 mmols) in CH_3CN (9.7 ml), at 0°C, was added slowly a solution of CAN (1.5 g, 4 eq) and $NaHCO_3$ (0.4 g, 7 eq) in water (7.8 ml). The solution was stirred at 0°C for 30 minutes after which it was poured in sat. aq. $NaHCO_3$. The aqueous layer was then extracted with CH_2Cl_2 (3x) and the combined organic extracts were dried over $MgSO_4$. The solids were filtered and the solvent evaporated. The crude quinone was then dissolved in dry toluene (7 ml) and acetoxybutadiene was added (0.4 ml, 5 eq). The solution was stirred for 18 hours. Silica gel was then added (1 g) and air was bubbled through the solution for 30 minutes. The silica gel was filtered through Celite and the solvent was evaporated. The brown oil obtained was purified by flash chromatography (silica gel, 1:1 hexanes/EtOAc) to give 115 mg (29%) of the titled tricyclic compound. ^{1}H NMR ($CDCl_3$): δ 8.12-8.02 (m, 2H, ArH), 7.76-7.73 (m, 2H, ArH), 4.91 (bs, 1H, NH), 5.92 (s, 1H, H-1), 5.52 (bs, 1H, NH), 4.62-4.47 (m, 3H, H-2' + H-5' + H-3), 4.17 (dd, 1H, J = 4.4, 10.9, H-1'), 3.83 (dd, 1H, J = 8.6, 10.9, H-1'), 3.56 (s, 3H, CO_2Me), 3.02 (dd, 1H, J = 4.0, 19.9, H-4), 2.51 (dd, 1H, J = 11.6, 19.9, H-4), 2.33 (s, 3H, COMe), 1.74-1.52 (m, 3H, CH_2-CH(Me)$_2$), 1.44 (s, 9H, t-Bu), 0.90 (d, 6H, J = 6.3, isopropyl).

Step 4: **(1S,2'S,3S,5'S)-Methyl-(1-O-[Serine-Leucine-Me ester]-5,10-dioxo-3,4,5,10-tetrahydro-1-H-naphtho [2,3-c] pyran-3-yl) ketone hydrochloride BCH-2000**

A solution of the Boc protected tricyclic from step 3 (example 17) (54 mg, 0.092 mmol) in 96% formic acid (1 ml) was stirred at room temperature for 2 hours. The formic acid was evaporated and the residue dissolved in 0.1 M HCl. The aqueous phase was washed with CH_2Cl_2 (2x) and the water was evaporated. The titled compound was obtained as a yellow oil was dried under high vacuum for 18 hours after which it had crystallized: 40 mg (83%).

^{1}H NMR (DMSO-d_6): δ 8.98 (bs, 1H, NH amide), 8.42 (bs, 3H, NH_3Cl), 8.06-7.98 (m, 2H, ArH), 7.93-7.87 (m, 2H, ArH), 5.82 (s, 1H, H-1), 4.61 (dd, 1H, J = 3.9, 11.4), 4.34-4.23 (m, 2H), 4.13 (m, 1H), 4.02 (dd, 1H, J = 5.7, 9.8), 3.61 (s, 3H, CO_2Me), 2.88 (dd, 1H, J = 3.9, 19.6, H-4), 2.47 (m, 1H, H-4 hidden under the DMSO peak), 2.30 (s, 3H, COMe), 1.62-1.49 (m, 3H, CH_2-CH(Me)$_2$), 0.88-0.82 (m, 6H, isopropyl).

Example 18: **Amino acid substituted naphthoquinone derivatives**



Step 1: **N-BOC-serine methyl ester**

To a solution of serine methyl ester hydrochloride (0.12 g, 0.78 mmol) in 1.6 ml of dry MeOH, at room temperature, under argon, were added successively triethylamine (10% solution, 0.16 ml) and $(BOC)_2O$ (0.19 g, 1.1 eq.) and the solution was stirred for 60 minutes. It was then poured in cold 2% HCl and the

aqueous layer was extracted with CH_2Cl_2 (3x). The combined organic extracts were dried over $MgSO_4$, the solids were filtered and the solvents evaporated to give 0.17 g (100%) of the titled compound as a clear oil.

^1H NMR ($CDCl_3$): δ 5.56 (bs, 1H, NH), 4.34 (m, 1H, $\underline{CH}$-CO_2Me), 3.88 (m, 2H, $\underline{CH_2}$-OH), 3.75 (s, 3H, CO_2Me), 2.96 (bs, 1H, OH), 1.44 (s, 9H, BOC).

Step 2: **(1S, 2'S, 3R) and (1R, 2'S, 3S)-1-[O-serine methyl ester]-3-aceto-5,8-dimethoxy isochroman.**

The titled compounds were obtained as per procedure described in step 2, example 17. They were purified via flash chromatography (silica gel, 2:1 hexanes/EtOAc). The mixture of isomers is not separable by chromatography.

^1H NMR ($CDCl_3$): δ 6.73 (m, 2H, ArH), 6.07+5.78 (2d, 1H, NH), 5.72+5.70 (2s, 1H, H-1), 4.56-4.35 (m, 3H, H-1' and H-2'), 3.98 (m, 1H, H-3), 3.90+3.81+3.78+3.77+3.76+3.67 (6s, 18H [6x3H], Ar-OMe and CO_2Me), 3.04 (2dd, 1H, H-4), 2.50 (2dd, 1H, H-4), 2.32 (d, 3H, $COCH_3$), 1.47+1.43 (2s, 9H, BOC).

Step 3: **(1S, 2'S, 3R) and (1R, 2'S, 3S)-methyl-(1-[O-N-BOC-serine methyl ester]-5,10-dioxo-3,4,5,10-tetrahydro-1-H-naphtho [2,3-C] pyran-3-yl) ketone.**

The same procedure as described in step 3, example 17, was used for the titled compound, which was purified via flash chromatography (silica gel, 2:1 hexanes/EtOAc).

The mixture of isomers is not separable by chromatography.

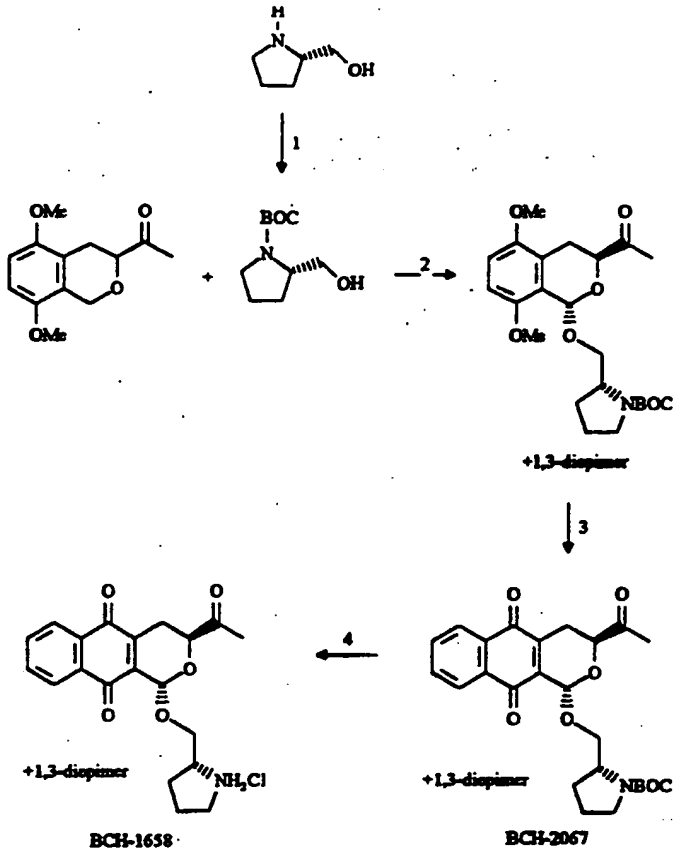
^1H NMR ($CDCl_3$): δ 8.05 (m, 2H, ArH), 7.73 (m, 2H, ArH), 5.90+5.52 (2d, 1H, NH), 5.73+5.72 (2s, 1H, H-1), 4.60-4.05 (m, 4H, H-3, H-1' and H-2'), 3.81+3.70 (2s, 3H, CO_2CH_3), 3.01 (2m, 1H, H-4), 2.48 (m, 1H, H-4), 2.35 (2s, 3H, $COCH_3$), 1.47+1.43 (2s, 9H, BOC).

Step 4: **(1S, 2'S, 3R) and (1R, 2'S, 3S)-methyl-(1-[O-serine methyl ester]-5,10-dioxo-3,4,5,10-tetrahydronaphtaleno [2,3-C] pyran-3-yl) ketone hydrochloride.**

The titled compounds were obtained as per procedure described in step 4, example 17.

^1H NMR (DMSO): δ 8.05-7.82 (m, 4H, ArH), 5.83+5.78 (2s, 1H, H-1), 4.69-4.40 (m, 2H, H-1'), 4.27 (m, 1H, H-3), 4.16 (m, 1H, H-2'), 3.79+3.73 (2s, 3H, CO_2Me), 2.91+2.87 (2m, 1H, H-4), 2.50 (m, 1H, H-4), 2.31+2.29 (2s, 3H, $COCH_3$).

Example 19: **Amino alcohol substituted naphthoquinone derivative**



Step 1: **N-BOC-Prolinol**

The titled compound was obtained as per procedure described in step 1, example 18.
^{1}H NMR ($CDCl_3$): δ 4.19 (bs, 1H, OH), 3.95 (m, 1H, H-2), 3.59 (m, 2H, $\underline{CH_2}$-OH), 3.42 (m, 1H, H-5), 3.30 (m, 1H, H-5), 2.01 (m, 1H, H-3), 1.83 (m, 2H, H-4), 1.60 (m, 1H, H-3), 1.45 (s, 9H, BOC).

Step 2: **(1S, 2'S, 3R) and (1R, 2'S, 3S)-1-[O-N-BOC-prolinol]-3-acetyl-5,8-dimethoxy isochroman**

The titled compounds were obtained as per procedure described in step 2, example 17. They were purified via flash chromatography (silica gel, 7:3 hexanes/EtOAc). The mixture of isomers is not separable by chromatography.
^{1}H NMR ($CDCl_3$): δ 6.72 (m, 2H, ArH), 5.82+5.77 (2s, 1H, H-1), 4.54 (m, 1H, H-3), 4.18-3.20 (m, 5H, H-1', H-2' and H-5'), 3.82+3.79 (2s, 6H, ArOMe), 3.05 (2m, 1H, H-4), 2.53 (m, 1H, H-4), 2.31 (s, 3H, $COCH_3$), 2.07-1.75 (m, 4H, H-3' and H-4'), 1.46 (s, 9H, BOC).

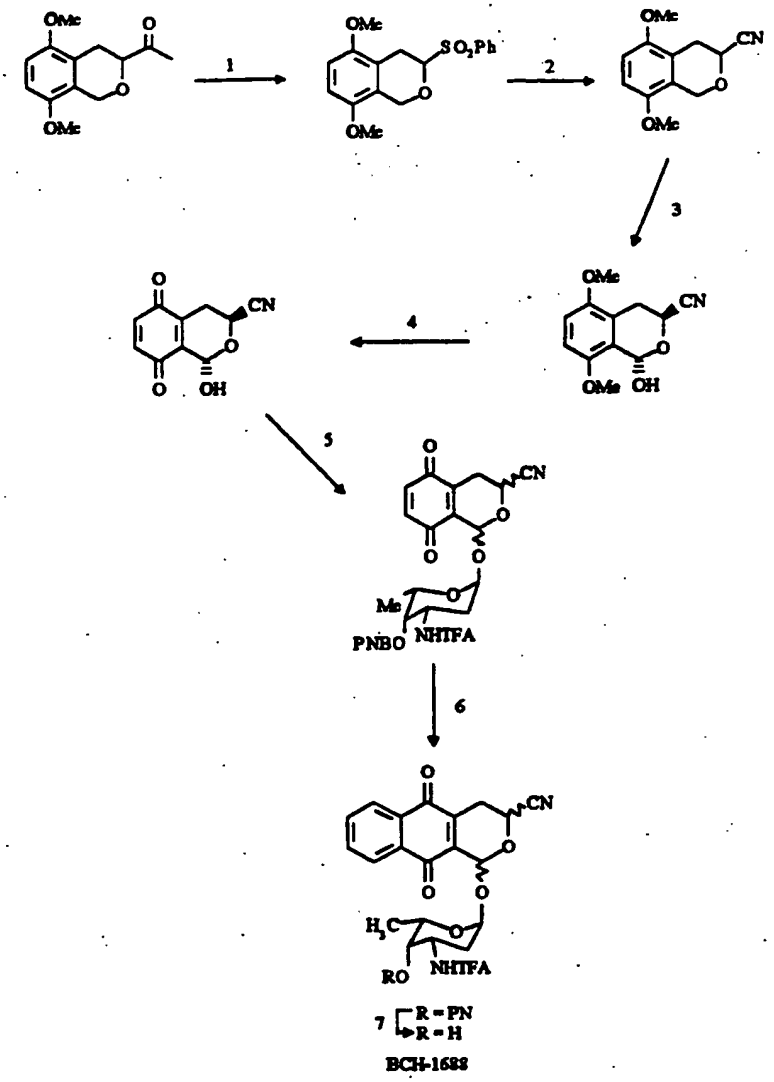
Step 3: **(1S, 2'S, 3R) and (1R, 2'S, 3S)-methyl-(1-[O-N-BOC-prolinol]-5,10-dioxo-3,4,5,10-tetrahydro-1-H-naphtho [2,3-C] pyran-3-yl) ketone BCH-2067**

The titled compounds were obtained as per procedure described in step 3, example 17. They were purified via preparative thin layer chromatography (silica gel, 7:3 hexanes/ethyl acetate).
^{1}H NMR ($CDCl_3$): δ 8.02 (m, 2H, ArH), 7.70 (m, 2H, ArH), 5.75+5.73 (2s, 1H, H-1), 4.47 (m, 1H, H-3), 4.15-3.18 (m, 5H, H-1', H-2' and H-5'), 2.97 (2m, 1H, H-4), 2.5 (m, 1H, H-4), 2.33+2.32 (2s, 3H, $COCH_3$), 2.05-1.72 (m, 4H, H-3' and H-4'), 1.48 (s, 9H, BOC).

Step 4: **(1S, 2'S, 3R) and (1R, 2'S, 3S)-methyl-(1-[O-prolinol]-3,4,5,12-tetrahydronaphtho-[2,3-C] pyran-3-yl) ketone hydrochloride salt.**

The titled compounds were obtained as per procedure described in step 4, example 17.
^{1}H NMR (DMSO): δ 8.02 (m, 2H, ArH), 7.88 (m, 2H, ArH), 5.73+5.71 (2s, 1H, H-1), 4.68 (m, 1H, H-3), 4.19-3.48 (m, 3H, H-2' and H-1'), 3.10 (m, 2H, H-5'), 2.39 (dd, 1H, H-4), 2.35 (m, 1H, H-4), 2.32+2.31 (2s, 3H, $COCH_3$), 2.10-1.55 (m, 4H, H-3' and H-4').

Example 20: Preparation of naphtho-[2,3-c] pyran derivative with a cyano side chain



Step 1: 5,8-dimethoxy-3-phenylsulphone isochroman

To a stirred solution of 5,8-dimethoxy-3-aceto isochroman (12.8 g, 54 mmol) in methylene chloride (350 ml) at room temperature was added 3-chloroperbenzoic acid 80% (18 g, 83 mmol) in portions over 15 minutes. After 2 hours, magnesium sulfate (6.8 g, 56 mmol) and sulfinic acid (10 g, 70 mmol) were added. After 2 hours, a saturated solution of potassium carbonate was added then the reaction mixture was washed with water and brine. The organic layer was dried over $MgSO_4$ and evaporated. The titled compound was purified by trituration in ether (11 g, 60%), m.p.: 118-119°C.

^1H NMR (250 MHz, C_6D_6), δ: 7.99 (dd, J = 1.5 and 8.0 Hz, 2H, Ar-H), 6.90 (m, 3H, Ar-H), 6.29 (2d, J = 8.9 Hz, 2H, Ar-H), 5.08 (d, J = 15.5 Hz, 1H, H-1), 4.53 (d, J = 15.5 Hz, 1H, H-1), 4.40 (dd, J = 4.7 and 9.2 Hz, 1H, H-3), 3.40 (dd, J = 4.7 and 17.0 Hz, 1H, H-4), 3.28 (s, 3H, $-OCH_3$), 3.27 (dd, 9.2 and 17.0 Hz, 1H, H-4), 3.19 (s, 3H, $-OCH_3$).

Step 2: 5,8-dimethoxy-3-cyano isochroman

To a stirred solution of $AlCl_3$ (1.39 g, 10.4 mmol) and TMS-CN (1.4 ml, 10.4 mmol) in CH_2Cl_2 (40 ml) at -78°C under argon was added the pyranylsulfone from step 1 (example 2) (1.16 g, 3.5 mmol) then the temperature was slowly raised to -20°C. After 4 hours, the reaction mixture was worked up in methylene chloride and water. The organic layer was washed with brine and dried over $MgSO_4$. The solvent was evaporated and the residue was purified by flash chromatography (hexanes/AcOEt 3/1) to give the titled compound (596 mg, 78%).

^1H NMR (250 MHz, $CDCl_3$), δ: 6.30 (2d, J = 8.2 Hz, 2H, Ar-H), 5.08 (d, J = 16.3 Hz, 1H, H-1), 4.78 (d, J = 16.3 Hz, 1H, H-1), 4.03 (t, J = 5.1 Hz, 1H, H-3), 3.27 (s, 3H, $-OCH_3$), 3.18 (s, 3H, $-OCH_3$), 2.80 (dd, J = 5.1 and 17.2 Hz, 1H, H-4), 2.66 (dd, J = 5.1 and 17.2 Hz, 1H, H-4).

Step 3: 1-hydroxy-3-cyano-5,8-dimethoxy isochroman

To a stirred solution of 2,5-dimethoxy-3-cyano isochroman (670 mg, 3.06 mmol) in CCl_4 (60 ml) were added N-bromosuccinimide (653 mg, 3.67 mmol) and a catalytic amount of AIBN. The mixture was heated to reflux and after 45 minutes, the solvent was evaporated and tetrahydrofurane (40 ml) and water (40 ml) were added. After 1 hour, the reaction mixture was worked up in ether. The organic layer was washed with brine and dried over $MgSO_4$. The solvent was evaporated and the residue purified by trituration in a small amount of ether to give the titled compound (453 mg, 63%).

^1H NMR (250 MHz, acetone D_6): 6.90 (2d, J = 9.0 Hz, 2H, Ar-H), 6.06 (2d, J = 5.2 Hz, 2H, H-1, -OH), 5.27 (dd, J = 4.1 and 12.1 Hz, 1H, H-3), 3.81 (s, 3H, $-OCH_3$), 3.78 (s, 3H, $-OCH_3$), 3.09 (dd, J = 4.1 and 17.1 Hz, 1H, H-4), 2.82 (dd, J = 12.1 and 17.1 Hz, 1H, H-4).

Step 4: 1-hydroxy-3-cyano-5,8-dioxo-5,8-dihydroisochroman

The titled compound was obtained in 77% yield by applying the procedure described in step 3, example 12, to the precursor of step 3 of this example.

^1H NMR (250 MHz, acetone D_6) δ: 6.86 (2d, J = 10.1 Hz, 2H, -CH=CH-), 6.61 (d, J = 5.7 Hz, 1H, H-1), 5.88 (d, J = 5.7 Hz, 1H, -OH), 5.20 (dd, J = 3.8 and 11.6 Hz, 1H, H-3), 2.98 (dd, J = 3.8 and 18.9 Hz, 1H, H-4), 2.73 (dd, J = 11.6 and 18.9 Hz, 1H, H-4).

Step 5 and 6: (1'S, 1S, 3R) and (1'S, 1R, 3S)-5,10-dioxo-3-cyano-1-(2',3',6',-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1-H-naphtho-[2,3-c] pyran

The titled compounds were obtained in 27% yield by following the procedure described in step 4, example 12, on the precursor of step 4 of this example.

^1H NMR (250 MHz, CD_2Cl_2) δ: 8.30 (m, 4H, Ar-H), 8.10 (m, 2H, Ar-H), 7.80 (m, 2H, Ar-H), 6.55 (m, 1H, -NH), 6.15 and 5.95 (2s, 1H, H-1), 5.70 (m, 1H, H-4'), 5.60 and 5.55 (m, 1H, H-1'), 5.10 (m,

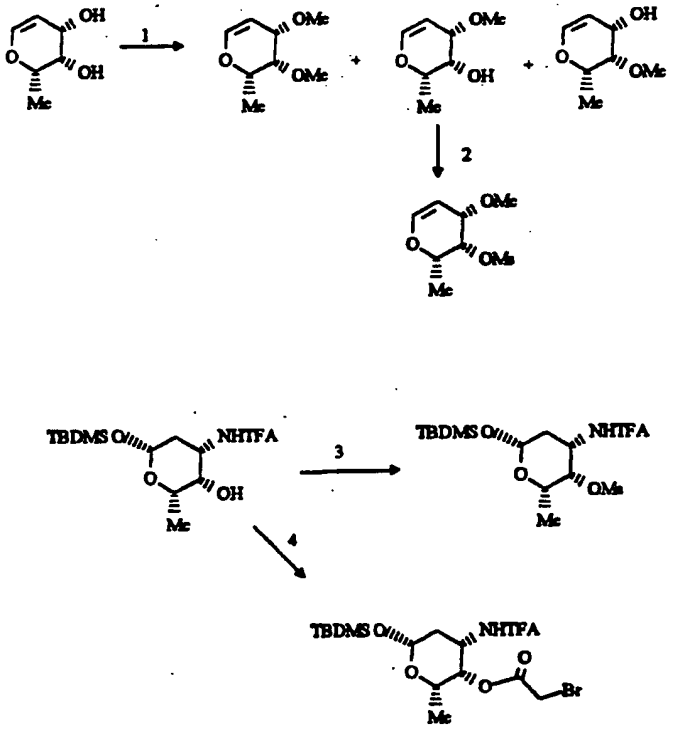
1H, H-3), 4.70-4.20 (m, 2H, H-3', H-5'), 3.25-2.80 (m, 2H, H-4), 2.40-2.00 (m, 2H, H-2'), 1.30 and 1.20 (2d, J = 6.7 Hz, 3H, H-6').

Step 7: **(1'-S, 1-R, 3-S) and (1'-S, 1-S, 3-R)-3-cyano-1-[2',3',6'-trideoxy-3'-trifluoroacetamido-4'-hydroxy-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-C] pyran-3-yl BCH-1688**

The titled compounds were obtained in 63% yield by following the procedure described in step 3, example 5, on the precursor from step 6 of this example.

^{1}H NMR (250 MHz, CD_2Cl_2) δ: 8.07 (m, 2H, Ar-H), 7.79 (m, 2H, Ar-H), 6.80 (m, 1H, N-H), 6.09 and 5.92 (2s, 1H, H-1), 5.52 and 5.42 (2d, 1H, H-1'), 5.04 (1m, 1H, H-3), 4.40-4.05 (m, 2H, H-3', H-5'), 3.70 (m, 1H, H-4'), 3.20-3.05 (1m, 1H, H-4), 3.00-2.80 (1m, 1H, H-4), 2.30-2.00 (m, 3H, -OH, H-2'), 1.38 and 1.29 (2d, J = 6.7 Hz, 3H, H-6').

Example 21: **Preparation of some sugar derivatives**



Step 1: **3,4-dimethoxy-L-fucal, and 3-methoxy-L-fucal**

To a stirred solution of L-fucal (400 mg, 3.1 mmol) in dimethylformamide (7.5 ml) were added methyl iodide (0.85 ml, 3.6 mmol) and silver oxide (1.16 g, 5.0 mmol). After 1.5 hour, the reaction mixture was worked up in CH_2Cl_2 and water. The organic layer was washed with brine and dried over $MgSO_4$. The solvent was evaporated. The products were separated by flash chromatography (hexanes/AcOEt 2/1) to give dimethoxy fucal (79 mg, 16%).

^1H NMR (250 MHz, $CDCl_3$) δ: 6.29 (dd, J = 1.3 and 6.2 Hz, 1H, H-1), 4.72 (m, 1H, H-2), 4.05 (m, 2H, H-5, H-4), 3.57 (s, 3H, $-OCH_3$), 3.44 (m, 1H, H-3), 3.39 (s, 3H, $-OCH_3$), 1.31 (d, J = 6.6 Hz, 3H, H-6).

The 3-methoxy-L-fucal (20% yield) had:

^1H NMR (250 MHz, $CDCl_3$) δ: 6.36 (dd, J = 1.2 and 6.2 Hz, 1H, H-1), 4.60 (m, 1H, H-2), 4.05-3.80 (m, 3H, H-3, H-4, H-5), 3.40 (s, 3H, $-OCH_3$), 2.37 (d, J = 3.9 Hz, 1H, -OH), 1.36 (d, J = 6.6 Hz, 3H, H-6).

Step 2: **3-methoxy-4-mesyl-L-fucal**

Mesylation of 3-methoxy-L-fucal yielded (84%) of the titled compound.

^{1}H NMR (250 MHz, $CDCl_3$) δ: 6.34 (dd, J = 2.1 and 6.5 Hz, 1H, H-1), 4.95 (m, 1H, H-2), 4.73 (m, 1H, H-4), 4.13 (m, 2H, H-3, H-5), 3.45 (s, 3H, $-OCH_3$), 3.15 (s, 3H, $-SO_2CH_3$), 1.40 (d, J = 6.6 Hz, 3H, H-6).

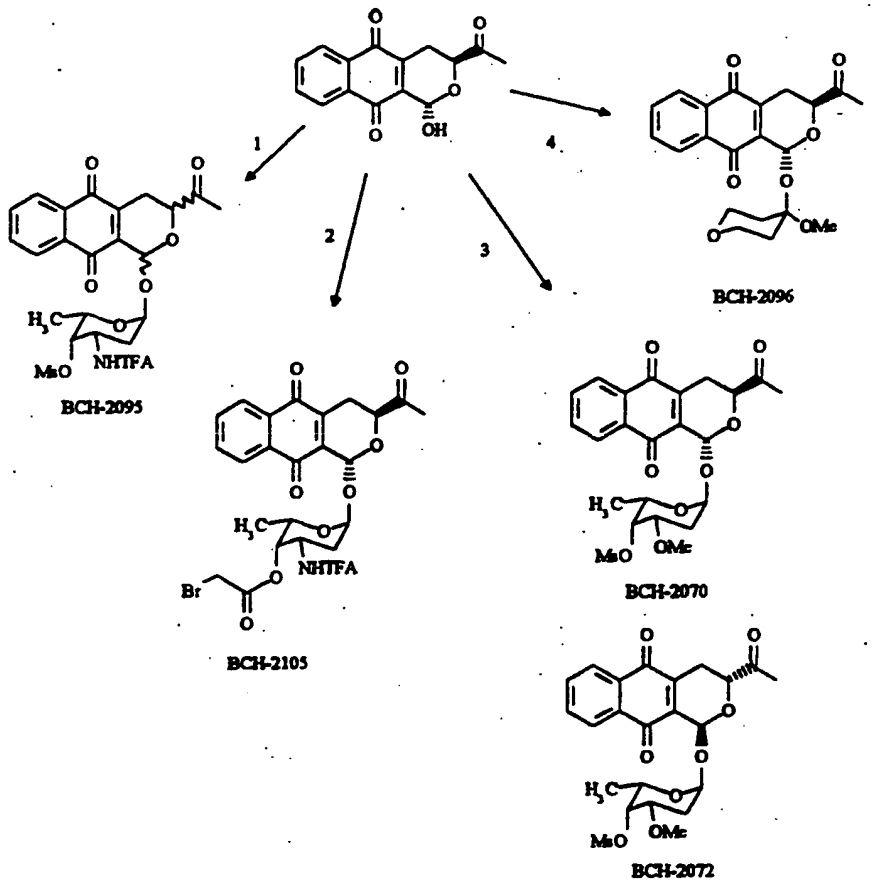
Step 3: **1-t-Butyl dimethylsilyloxy-3-trifluoroacetamido-4-methanesulfonyl-2,3,6-trideoxy-L-lyxohexopyranose**

To a stirred solution of 1-t-butyl dimethylsilyloxy, 3-trifluoroacetamido-2,3,6-trideoxy-L-lyxohexopyranose (504 mg, 1.41 mmol) in CH_2Cl_2 (7 ml) at 0°C were added methanesulfonyl chloride (218 µl, 2.82 mmol) and triethylamine (590 µl, 4.2 mmol). After 2 hours the reaction mixture was worked up with CH_2Cl_2 and HCl 0.1 N. The organic layer was washed with a solution of $NaHCO_3$ and brine then dried over $MgSO_4$. The solvent was evaporated to give 1-t-butyl dimethyl silyloxy, 3-trifluoroacetamido-2,3,6 trideoxy-4 methanesulfonyl-L-lyxohexopyranose (604 mg, 98%).
^{1}H NMR (250 MHz, $CDCl_3$) δ: 7.28 (d, J = 7.7 Hz, 1H, N-H), 4.83 (dd, J = 2.1 and 9.1 Hz, 1H, H-1), 4.71 (d, J = 2.2 Hz, 1H, H-4), 4.25 (m, 1H, H-3), 3.75 (q, J = 6.4 Hz, 1H, H-5), 3.18 (s, 3H, $-SO_2-CH_3$), 2.0 (m, 1H, H-2), 1.75 (m, 1H, H-2), 1.31 (d, J = 6.4 Hz, 3H, H-6), 0.89 (s, 9H, $-C(CH_3)_3$), 0.12 and 0.11 (2s, 6H, $-Si(CH_3)_2$).

Step 4: **1-t-Butyl dimethylsilyloxy-3-trifluoroacetamido-4-O-bromoacetyl-2,3,6-trideoxy-L-lyxohexopyranose**

To a stirred solution of 1-t-butyl dimethylsilyloxy-3-trifluoroacetamido-2,3,6-trideoxy-L-lyxohexopyranose (81 mg, 0.18 mmol) in CH_2Cl_2 (2 ml) at 0°C were added collidine (47 µl, 0.36 mmol), and bromoacetylbromide (24 µl, 0.27 mmol). After 1 hour, the reaction mixture was worked up with CH_2Cl_2 and water. The organic layer was washed with brine and dried over $MgSO_4$. The solvent was evaporated to give the titled compound (76 mg, 74%).
^{1}H NMR (250 MHz, $CDCl_3$) δ: 6.47 (d, J = 8 Hz, 1H, N-H), 5.03 (d, J = 3.0 Hz, 1H, H-4), 4.84 (dd, J = 2.3 and 9.0 Hz, 1H, H-1), 4.35 (m, 1H, H-3), 4.00 and 3.80 (2d, J = 10.5 Hz, 2H, $-CH_2-Br$), 3.75 (dq, J = 1 Hz, 6.5 Hz, 1H, H-5), 2.05-1.70 (m, 2H, H-2), 1.20 (d, J = 6.5, 3H, -H6), 0.9 (s, 9H, $-C(CH_3)_3$), 0.13 (2s, 6H, $-Si(CH_3)_2$).

Example 22: **Preparation of few naphtho-[2,3-c] pyran derivatives**



Step 1: **(1'-S, 1-S, 3-R) and (1'-S, 1-R, 3-S)-methyl-(1-[2',3',4',6' tetradeoxy-3'-trifluoroacetamido-4'-O-methane-sulfonyl-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10 tetrahydronaphtho-[2,3-c] pyran-3-yl) ketone BCH-2095**

The titled compound was obtained in 45% yield by using the procedure described in step 2 of this example but with the sugar obtained from step 3, example 21. It was purified by flash chromatography (toluene/acetone 95/5).

^{1}H NMR (250 MHz, $CDCl_3$) δ: 8.10 (m, 2H, Ar-H), 7.80 (m, 2H, Ar-H), 7.15 (2d, J = 8.0 Hz, 1H, N-H), 6.16 and 6.00 (2s, 1H, H-1), 5.62 and 5.50 (2d, J = 1.5 Hz, 1H, H-1'), 4.89 and 4.84 (2 broad s, 1H, H-4'), 4.75 and 4.25 (2q, J = 6.6 Hz, H-5'), 4.50 (m, 2H, H-3, H-3'), 3.23 and 3.21 (2s, 3H, $-SO_2CH_3$), 3.10 (m, 1H, H-4), 2.55 (m, 1H, H-4), 2.33 and 2.32 (2s, 3H, $-CO-CH_3$), 2.00 (m, 2H, H-2'), 1.45 and 1.30 (2d, J = 6.6 Hz, H-6').

Step 2: **(1'-S, 1-S, 3-R)-methyl-(1-[2',3',4',6' tetradeoxy-3'-trifluoroacetamido-4'-O-(2-bromo-acetyl)-L-lyxopyranose]-5, 10-dioxo-3,4,5,10 tetrahydronaphtho-[2,3-c] pyran-3-yl) ketone BCH-2105**

To a stirred solution of the aglycone from example 3 (30 mg, 0.11 mmol), 4-bromoacetyl-1-t-butyl dimethylsilyloxy-3-trifluoro-acetamido daunosamine derivative (76 mg, 0.13 mmol) molecular sieves Å (62 mg) in CH_2Cl_2 (1.2 ml) at -50°C under argon was added trimethylsilyl trifluoromethanesulfonate (23 µl, 0.12 mmol). After 2 hours at -30°C, the reaction mixture was worked up with a solution of $NaHCO_3$ 10% and CH_2Cl_2. The organic layer was washed with brine and dried over $MgSO_4$, the residue was purified by flash chromatography (hexanes/AcOEt 2:1) to give the titled compound (8 mg, 12%).
^1H NMR (250 MHz, $CDCl_3$) δ: 8.12 (m, 2H, Ar-H), 7.77 (m, 2H, Ar-H), 6.33 (d, J = 8.1 Hz, 1H, N-H), 6.00 (s, 1H, H-1), 5.67 (s, 1H, H-1'), 5.16 (s, 1H, H-4'), 4.53 (dd, J = 3.9 and 11.6 Hz, 1H, H-3), 4.53 (m, 1H, H-3'), 4.23 (q, J = 6.7 Hz, 1H, H-5'), 3.90 (2d, J = 10.9 Hz, 2H, $-CH_2-Br$), 3.08 (dd, J = 3.9 and 19.8 Hz, 1H, H-4), 2.53 (dd, J = 11.6 and 19.8 Hz, 1H, H-4), 2.34 (s, 3H, $-CO-CH_3$), 2.02 (m, 2H, H-2'), 1.19 (d, J = 6.7 Hz, 3H, H-6').

Step 3: (1'-S, 1-R, 3-S)-methyl-(1-[2',3',4',6' tetradeoxy-3'-methoxy-4'-O-methanesulfonyl-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10 tetrahydronaphtho-[2,3-c] pyran-3-yl) ketone BCH-2070

The titled compound was obtained in 22% yield by applying the procedure described in step 4, example 12, to the aglycone from example 3 and the glycal from step 2, example 21. Purification was carried out by flash chromatography (toluene/acetone:95/5) M.P. 85-89°C.
^1H NMR (250 MHz, $CDCl_3$) δ: 8.11 (m, 2H, Ar-H), 7.77 (m, 2H, Ar-H), 5.98 (s, 1H, H-1), 5.62 (d, J = 2.8 Hz, 1H, H-1'), 4.85 (s, 1H, H-4'), 4.46 (dd, J = 4.0 and 11.6 Hz, 1H, H-3), 4.04 (q, J = 6.5 Hz, 1H, H-5'), 3.62 (m, 1H, H-3'), 3.39 (s, 3H, $-OCH_3$), 3.14 (s, 3H, $-SO_2-CH_3$), 3.05 (dd, J = 4.0 and 19.5 Hz, 1H, H-4), 2.50 (dd, J = 11.6 and 19.5 Hz, 1H, H-4), 2.33 (s, 3H, $-CO-CH_3$), 2.00 (m, 2H, H-2'), 1.33 (d, J = 6.5 Hz, 3H, H-6').

Step 3 (Cont'd): (1'-S, 1'S, 3-R)-methyl-(1-[2',3',4',6' tetradeoxy-3'-methoxy-4'-O-methanesulfonyl-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10 tetrahydronaphtho-[2,3-c] pyran-3-yl) ketone BCH-2072

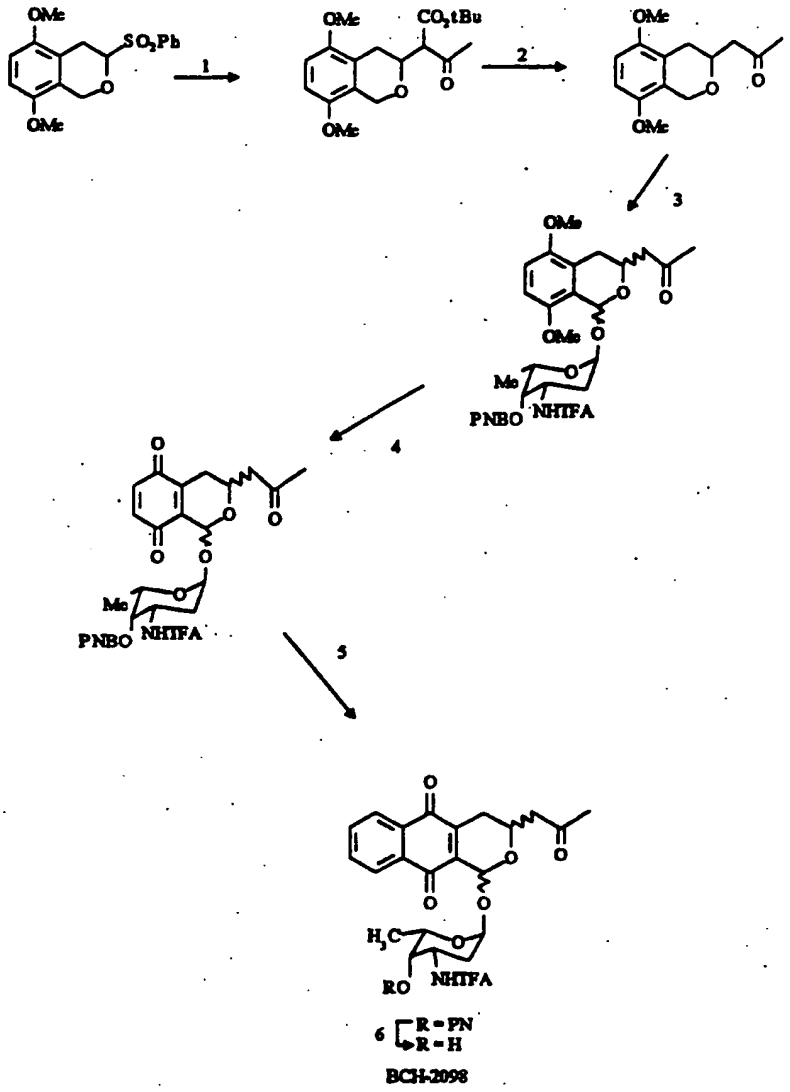
The titled compound was obtained in 11% yield by using the procedure described in step 3 of this example but using the 1,3-diepimeric aglycone. M.P. 139-141°C.
^1H NMR (250 MHz, $CDCl_3$) δ: 8.12 (m, 2H, Ar-H), 7.77 (m, 2H, Ar-H), 6.15 (s, 1H, H-1), 5.52 (d, J = 1.5 Hz, 1H, H-1'), 4.95 (d, J = 1.5 Hz, 1H, H-4'), 4.59 (q, J = 6.5 Hz, 1H, H-5'), 4.49 (dd, J = 4.1 and 11.6 Hz, 1H, H-3), 3.60 (m, 1H, H-3'), 3.38 (s, 3H, $-SO_2CH_3$), 3.15 (s, 3H, $-OCH_3$), 3.07 (dd, J = 4.1 and 19.9 Hz, 1H, H-4), 2.55 (dd, J = 11.6 and 19.9 Hz, 1H, H-4), 2.33 (s, 3H, $-CO-CH_3$), 1.95 (m, 2H, H-2'), 1.50 (d, J = 6.5 Hz, 3H, H-6').

Step 4: **(1-S, 3-R) and (1-R, 3-S)-methyl-(1-(1-methoxy-4-oxocyclohexyloxy)-5,10-dioxo-3,4,5,10 tetrahydronaphtho-[2,3-c] pyran-3-yl) ketone BCH-2096**

To a stirred solution of the aglycone from example 3 (7 mg, 0.026 mmol) in tetrahydrofurane (1.6 ml) were added 5,6-dihydro-4-methoxy-2H-pyran (29 µl, .26 mmol) and a catalytic amount of PTSA. After 4 hours, the reaction was worked up with CH_2Cl_2 and $NaHCO_3$ 5%. The organic layer was washed with brine and dried over $MgSO_4$. The solvent was evaporated to give the titled compound (10 mg, 96%).

^1H NMR (250 MHz, $CDCl_3$) δ: 8.10 (m, 2H, Ar-H), 7.70 (m, 2H, Ar-H), 6.34 (s, 1H, H-1), 4.66 (dd, J = 4.3 and 11.6 Hz, 1H, H-3), 3.80-3.50 (m, 4H, $-CH_2-O-CH_2-$), 3.40 (s, 3H, $-OCH_3$), 3.06 (dd, J = 4.3 and 19.7 Hz, 1H, H-4), 2.52 (dd, J = 11.6 and 19.0 Hz, 1H, H-4), 2.30 (s, 3H, $-CO-CH_3$), 2.20-1.85 (m, 4H, $-CH_2-C-CH_2-$).

Example 23: **Preparation of naphtho-[2,3-c] pyran derivative with a homo methyl ketone side chain.**



Step 1: **5,8-Dimethoxy-3-(t-butyl acetoacetato) isochroman**

To a stirred solution of pyranosulfone from step 1, example 20, (1.12 g, 3.35 mmol) in CH_2Cl_2 (40 ml) at -78°C were added a solution of silyl enol ether of t-butyl acetoacetate (10 mmol) in CH_2Cl_2 (10 ml) and $AlCl_3$ (1.33 g, 10 mmol). Temperature was then raised to -30°C for 2 hours. The reaction mixture was worked up with CH_2Cl_2 and HCl 0.1 N. The organic was washed with brine and dried over $MgSO_4$. The solvent was evaporated to give the title β-ketoester (519 mg, 43%).

^1H NMR (250 MHz, $CDCl_3$), δ: 6.63 (m, 2H, Ar-H), 4.91 and 4.85 (2d, J = 9.8 Hz, 1H, H-1), 4.60 and 4.53 (2d, J = 7.9 Hz, 1H, H-1), 4.20 (m, 1H, H-3), 3.76-3.74 (3s, 6H, $-OCH_3$), 3.62 (t, J = 9.5

Hz, 1H), 2.90 (m, 1H, H-4), 2.45 (m, 1H, H-4), 2.32 and 2.28 (2s, 3H, -CO-CH_3), 1.49 and 1.47 (2s, 9H, -$C(CH_3)_3$).

Step 2: 5,8-Dimethoxy-3-(propane-2-one) isochroman

The product from step 1 of this example was decarboxylated, in 91% yield, with concentrated aqueous HBr in acetone.

^{1}H NMR (250 MHz, $CDCl_3$) δ: 6.63 (2d, J = 9.0 Hz, 2H, Ar-H), 4.88 (d, J = 15.9 Hz, 1H, H-4), 4.58 (d, J = 15.9 Hz, 1H, H-4), 4.06 (m, 1H, H-3), 3.77 and 3.75 (2s, 6H, -OCH_3), 2.85 (m, 2H, -CH_2-CO-), 2.63 (dd, J = 4.8 and 16.5 Hz, 1H, H-4), 2.40 (dd, J = 10.9 and 16.5 Hz, 1H, H-4), 2.24 (s, 3H, -CO-CH_3).

Step 3: 5,8-Dimethoxy-3-(propane-2-one)-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-isochroman

The isochroman from 2 herein was glycosidated as per procedure described in step 3, example 34. The title compound was obtained in 97% yield.

^{1}H NMR (250 MHz, $CDCl_3$) δ: 8.26 (d, J = 2.0 Hz, 4H, Ar-H), 6.74 (m, 2H, Ar-H), 6.50 and 6.35 (2d, J = 7.0 Hz, 1H, -NH), 6.02 and 5.88 (2s, 1H, H-1), 5.59 (s, 1H, H-1'), 5.49 and 5.46 (2s, 1H, H-4'), 4.70 (m, 2H, H-3', H-3), 3.80 and 3.78 (2s, 6H, -OCH_3), 3.00-2.50 (m, 2H, H-4, -CH_2-CO-), 2.50-2.00 (m, 2H, H-4, -CH_2-CO-), 2.24 and 2.22 (2s, 3H, -CO-CH_3), 1.25 and 1.15 (2d, J = 6.5 Hz, 3H, H-6').

Step 4: 5,8-Dioxo-3-(propane-2-one)-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-isochroman

The titled compound was obtained in 94% yield via oxidative demethylation of the isochroman obtained from step 3 herein as per procedure described in step 4, example 34.

^{1}H NMR (250 MHz, $CDCl_3$), δ: 8.30 (d, J = 5.7 Hz, 4H, ArH), 6.80 (m, 2H, Ar-H), 6.42 and 6.35 (2d, J = 7.0 Hz, 1H, N-H), 5.81 and 5.70 (2s, 1H, H-1), 5.59 and 5.54 (2s, 1H, H-1'), 5.45 (2d, J = 1.5 Hz, 1H, H-4'), 4.80-4.40 (m, 3H, H-3', H-5', H-3), 2.90 (m, 1H, H-4), 2.70 (m, 2H, -CH_2-CO), 2.40-1.90 (m, 3H, H-4, H-2'), 2.23 and 2.21 (2s, 3H, -CO-CH_3), 1.28 and 1.15 (2d, J = 6.5 Hz, 3H, H-6').

Step 5: 5,10-Dioxo-3-(propane-2-one)-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c] pyran

The titled compound was obtained via cycloaddition between 1-acetoxybutadiene and the quinone from step 4 herein by following the procedure described in step 5, example 34.

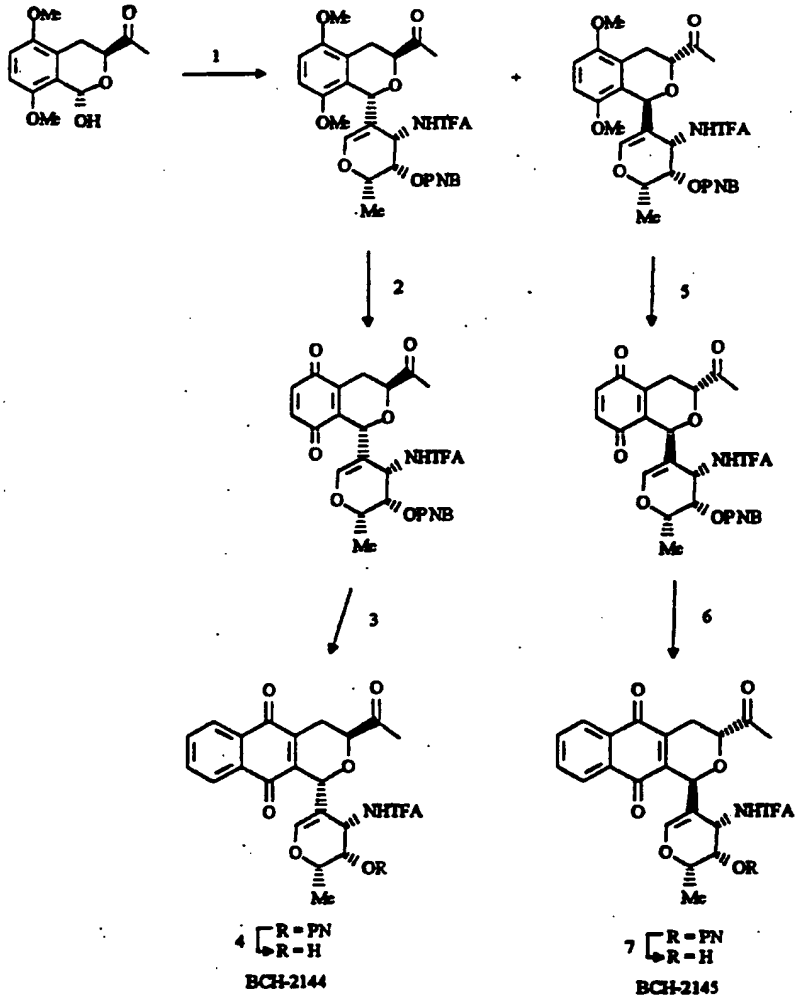
^{1}H NMR (250 MHz, $CDCl_3$), δ: 8.31 (2d, J = 9.1 Hz, 4H, Ar-H), 8.11 (m, 2H, Ar-H), 7.78 (m, 2H, Ar-H), 6.45 and 6.33 (2d, J = 7.3, 1H, N-H), 5.99 and 5.88 (2s, 1H, H-1), 5.71 and 5.60 (2s, 1H, H-1'), 5.48 (1s, 1H, H-4'), 4.80-4.40 (m, 3H, H-3, H-3', H-4'), 3.00-2.60 (m, 3H, H-4, -CH_2-CO-), 2.50-2.00 (m, 3H, H-4, H-2'), 2.25 and 2.23 (2s, 3H, -CO-CH_3), 1.33 and 1.17 (2d, J = 6.5 Hz, 3H, H-6').

Step 6: **(1'-S, 1-S, 3-R) and (1'-S, 1-R, 3-S)-1-(6-hydroxy-1-(2',3',6'-trideoxy-3'-trifluoroacetamido,4-hydroxy-L-lyxopyranose)-5,10-dioxo-3,4,5,10 tetrahydronaphtho-[2,3-c] pyran-3-yl) propane-2-one BCH-2098**

The titled compound was obtained following deprotection of the glycoside from step 5 herein as per procedure described in step 6, example 34.

^{1}H NMR (250 MHz, $CDCl_3$) δ: 8.10 (m, 2H, Ar-H), 7.75 (m, 2H, Ar-H), 6.73 (d, J = 7.5 Hz, 1H, N-H), 5.93 and 5.81 (2s, 1H, H-1), 5.52 and 5.41 (2d, J = 2.7 Hz, 1H, H-1'), 4.80-4.20 (m, 3H, H-3, H-3', H-5'), 3.70 (m, 1H, H-4'), 3.00-2.60 (m, 3H, H-4, -CH_2-CO-), 2.40-1.70 (m, 4H, H-4, H-2', -OH), 2.23 and 2.20 (2s, 3H, -CO-CH_3), 1.41 and 1.20 (2d, J = 6.6 Hz, 3H, H-6').

Example 24: **Preparation of naphtho-[2,3-c] pyran derivative with a C-2' glycoside linkage**



Step 1: **(1R, 3S) and (1-S, 3R)-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzyloxy-1,5-dihydro-L-lyxohexo-pyranose-2-yl)-5,8-dimethoxy-3-acetoisochroman**

2,5-Dimethoxy-1-hydroxy-3-acetoisochroman was reacted with 1,4-di-O-p-nitrobenzoyl-N-trifluoroacyl daunosamine as per procedure from step 1, example 5. The titled products were separated by flash chromatography (CH_2Cl_2/acetone 99/1).

^1H NMR (250 MHz, $CDCl_3$) δ: 8.30 (m, 3H, Ar-H, N-H), 8.09 (d, J = 8.7 Hz, 2H, Ar-H), 6.71 (2d, J = 8.8 Hz, 2H, Ar-H), 6.02 (s, 1H, H-1'), 5.84 (d, J = 3.6 Hz, 1H, H-4'), 5.62 (s, 1H, H-1), 5.30 (m, 1H, H-3'), 4.45 (m, 2H, H-3, H-5'), 3.81 (1s, 3H, $-OCH_3$), 3.76 (1s, 3H, $-OCH_3$), 3.11 (dd, J = 3.9 Hz and 17.3 Hz, 1H, H-4), 2.61 (dd, J = 12.1 and 17.3 Hz, 1H, H-4), 1.95 (s, 3H, $-COCH_3$), 1.28 (d, J = 6.6 Hz, 3H, H-6').

The second diastereomer had:

^{1}H NMR (250 MHz, $CDCl_3$) δ: 8.28 (2d, J = 9.0 Hz, 4H, Ar-H), 6.90 (d, J = 7.8 Hz, 1H, N-H), 6.70 (2d, J = 9.0 Hz, 2H, Ar-H), 6.18 (d, J = 1.5 Hz, 1H, H-1'), 5.75 (d, J = 4.8 Hz, 1H, H-4'), 5.55 (s, 1H, H-1), 5.30 (m, 1H, H-3'), 4.30 (m, 2H, H-5', H-4), 3.80 (s, 3H, -OCH_3), 3.60 (s, 3H, -OCH_3), 3.02 (dd, J = 4.3 and 17.6 Hz, 1H, H-4), 2.57 (dd, J = 11.6 and 17.6 Hz, 1H, H-4), 2.29 (s, 3H, -CO-CH_3), 1.29 (d, J = 6.6 Hz, 3H, H-6').

Step 2: **(1R, 3S)-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzyloxy-1,5-dihydro-L-lyxohexopyranose-2-yl)-5,8-dioxoisochroman**

The (1R, 3S) product from step 1 herein was oxidatively demethylated as per procedure in step 3, example 12.

^{1}H NMR (250 MHz, $CDCl_3$) δ: 8.23 (d, J = 8.7 Hz, 2H, Ar-H), 8.03 (d, J = 8.7 Hz, 2H, Ar-H), 7.65 (d, J = 6.6 Hz, 1H, N-H), 6.75 (2d, J = 10.3 Hz, 2H, Ar-H), 6.28 (d, J = 1.4 Hz, 1H, H-1), 5.78 (d, J = 3.8 Hz, 1H, H-4'), 5.37 (s, 1H, H-1'), 5.21 (m, 1H, H-3'), 4.43 (q, J = 6.5 Hz, 1H, H-5'), 4.24 (dd, J = 3.8 and 11.2 Hz, 1H, H-3), 2.90 (dd, J = 3.8 and 19.5 Hz, 1H, H-4), 2.40 (ddd, J = 1.6, 11.2 and 19.5 Hz, 1H, H-4), 1.88 (s, 3H, -$COCH_3$), 1.26 (d, J = 6.5 Hz, 3H, H-6').

Step 3: **(1R, 3S)-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzyloxy-1,5-dihydro-L-lyxohexopyranose-2-yl)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho [2,3-c] pyran**

The quinone from step 2 herein was cycloadded with 1-acetoxybutadiene as per procedure from step 4, example 12. The product had:

^{1}H NMR (250 MHz, $CDCl_3$) δ: 8.30 (d, J = 8.7 Hz, 2H, Ar-H), 8.10 (m, 4H, Ar-H), 7.80 (m, 2H, Ar-H), 6.36 (d, J = 1.9 Hz, 1H, H-1), 5.86 (d, J = 3.9 Hz, 1H, H-4'), 5.60 (s, 1H, H-1'), 5.31 (m, 1H, H-3'), 4.49 (q, J = 6.6 Hz, 1H, H-5'), 4.35 (dd, J = 3.9 Hz, and 11.4 Hz, 1H, H-3), 3.12 (dd, J = 3.9 Hz and 19.4 Hz, 1H, H-4), 2.62 (ddd, J = 1.9, 11.4 Hz, 19.4 Hz, 1H, H-4), 1.98 (s, 3H, -CO-CH_3), 1.31 (d, J = 6.6 Hz, 3H, H-6').

Step 4: **(1R, 3S)-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-hydroxy-1,5-dihydro-L-lyxohexopyranose-2-yl)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c] pyran BCH-2144**

The tricyclic product from step 3 herein was deprotected as per procedure from step 3, example 5. The title product had:

^{1}H NMR (250 MHz, $CDCl_3$) δ: 8.20 (m, 2H, Ar-H), 7.75 (m, 3H, N-H, Ar-H), 6.25 (d, J = 1.7 Hz, 1H, H-1), 5.55 (s, 1H, H-1'), 5.11 (m, 1H, H-3'), 4.32 (dd, J = 4.0 Hz and 11.1 Hz, 1H, H-3), 4.23 (q, J = 6.5 Hz, 1H, H-5'), 4.05 (d, J = 3.7 Hz, 1H, H-4'), 3.00 (dd, J = 4.0 and 19.8 Hz, 1H, H-4), 2.59 (ddd, J = 1.7, 11.1 and 19.8 Hz, 1H, H-4), 2.28 (s, 3H, -CO-CH_3), 1.70 (broad s, 1H, -OH), 1.34 (d, J = 6.5 Hz, 3H, H-6').

Step 5: (1S, 3R)-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzyloxy-1,5-dihydro-L-lyxohexopyranose-2-yl)-5,8-dioxoisochroman

The (1S, 3R) product from step 1 herein was oxidatively demethylated as per procedure in step 3, example 12.

^{1}H NMR (250 MHz, $CDCl_3$) δ: 8.32 (d, J = 9.0 Hz, 2H, Ar-H); 8.20 (d, J = 9.0 Hz, 2H, Ar-H), 7.58 (d, J = 8.3 Hz, 1H, N-H), 6.80 (2d, J = 10.1 Hz, 2H, Ar-H), 6.46 (d, J = 1.3 Hz, 1H, H-1), 5.73 (d, J = 4.8 Hz, 1H, H-4'), 5.33 (d, J = 1.9 Hz, 1H, H-1'), 5.25 (m, 1H, H-3'), 4.35 (q, J = 6.6 Hz, 1H, H-5'), 4.20 (dd, J = 4.1 Hz and 10.5 Hz, 1H, H-3), 2.88 (dd, J = 4.1 and 19.9 Hz, 1H, H-4), 2.40 (ddd, J = 1.9, 10.5 and 19.9 Hz, 1H, H-4), 2.27 (s, 3H, -$COCH_3$), 1.32 (d, J = 6.6 Hz, 3H, H-6').

Step 6: (1S, 3R)-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzyloxy-1,5-dihydro-L-lyxohexopyranose-2-yl)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c] pyran

The quinone from step 5 herein was cycloadded with 1-acetoxybutadiene as per procedure from step 4, example 12. The titled product had:

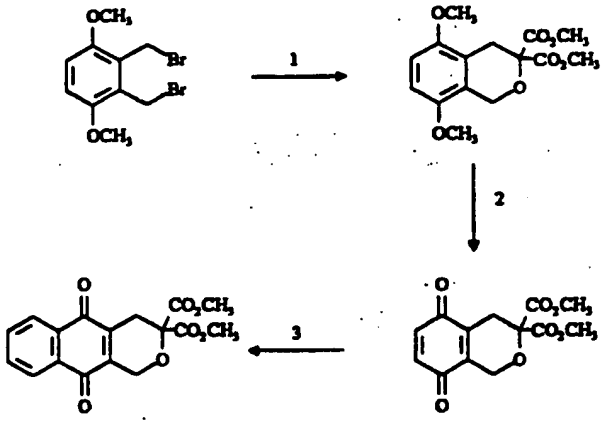
^{1}H NMR (250 MHz, $CDCl_3$) δ: 8.30 (d, J = 8.9 Hz, 2H, Ar-H), 8.22 (d, J = 8.9 Hz, 2H, Ar-H), 8.20 (m, 1H, Ar-H), 8.00 (m, 2H, N-H, Ar-H), 7.86 (m, 2H, Ar-H), 6.53 (s, 1H, H-1), 5.77 (d, J = 4.7 Hz, 1H, H-4'), 5.50 (s, 1H, H-1'), 5.30 (m, 1H, H-3'), 4.37 (q, J = 6.6 Hz, 1H, H-5'), 4.27 (dd, J = 4.0 and 10.7 Hz, 1H, H-3), 3.08 (dd, J = 4.0 and 19.8 Hz, 1H, H-4), 2.55 (ddd, J = 1.0, 10.7 and 19.8 Hz, 1H, H-4), 2.31 (s, 3H, -CO-CH_3), 1.31 (d, J = 6.6 Hz, 3H, H-6').

Step 7: (1S, 3R)-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-hydroxy-1,5-dihydro-L-lyxohexopyranose-2-yl)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c] pyran BCH-2145

The tricyclic product from step 6 herein was deprotected as per procedure from step 3, example 5. The titled product had:

^{1}H NMR (250 MHz, $CDCl_3$) δ: 8.19 (d, J = 8.9 Hz, 1H, N-H), 8.10 (d, J = 7.3 Hz, 1H, Ar-H), 7.90 (d, J = 7.3 Hz, 1H, Ar-H), 7.70 (m, 2H, Ar-H), 6.26 (s, 1H, H-1), 5.47 (s, 1H, H-1'), 5.10 (m, 1H, H-3'), 4.20 (m, 2H, H-3, H-5'), 3.97 (d, J = 4.0 Hz, 1H, H-4'), 3.00 (dd, J = 4.0 and 20.0 Hz, 1H, H-4), 2.55 (dd, J = 10.8 Hz, and 20.0 Hz, 1H, H-4), 2.32 (s, 3H, -CO-CH_3), 1.70 (broad s, 1H, -OH), 1.36 (d, J = 6.4 Hz, 3H, H-6').

Example 25: Preparation of 3,3-bis-(methoxycarbonyl)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran (BCH-1665)



BCH-1665

Step 1: 5,8-dimethoxy-3,3 bis (methoxycarbonyl)-isochroman

To a solution of 2,3 bis (bromomethyl)-1,4-dimethoxybenzene (1.30 g; 4.00 mmol) in 40 ml of a 1:1 mixture of tetrahydrofuran and dimethylformamide were added benzoyloxy-dimethylmalonate (1.06 g; 4.19 mmol), potassium carbonate (1.16 g; 8.38 mmol) and cesium carbonate (1.37 g; 4.19 mmol). The resulting mixture was stirred at 80°C (oil bath temperature) for 2.5 hours. It was then cooled to room temperature and filtered on a pad of silica gel and the solvents were evaporated using a vacuum pump to yield 2.3 g of crude alkylated product which was dissolved in methanol (60 ml). To this solution was added a solution of sodium methoxyde in methanol (4.57 ml; 4.37 M; 5 eq). The resulting mixture was stirred at room temperature for 2 hours and was then concentrated to a volume of ~10 ml. It was quenched with 1 N HCl and extracted with dichloromethane. The combined organic layers were washed with brine and dried over $MgSO_4$. The crude product was purified by column chromatography on silica gel using 10-25% ethyl acetate in hexane to afford the title compound (452 mg; 36% overall):
^1H NMR (250 MHz; $CDCl_3$) δ: 3.25 (2H, s, H-4), 3.72, 3.78, 3.79 (12H, 3s, 4xOCH_3), 4.88 (2H, s, H-1), 6.59 and 6.65 (2H, AB doublets, Ar-H).

Step 2: 5,8-dioxo-3,3 bis (methoxycarbonyl)-5,8-dihydro-isochroman

To a solution of 5,8-dimethoxy-3,3 bis (methoxycarbonyl)-isochroman (70 mg; 0.23 mmol) in acetonitrile (5 ml) at room temperature was added dropwise a solution of ceric ammonium nitrate (378 mg; 0.69 mmol) in water (1 ml). The resulting mixture was then stirred at room temperature for 5 minutes and was quenched by adding saturated sodium bicarbonate solution. The product was extracted with dichloromethane and the combined organic layers were washed with brine and dried over $MgSO_4$. Evaporation afforded the crude quinone (60 mg; 95%) which was used without further purification:
^1H NMR ($CDCl_3$, 250 MHz) δ: 3.03 (2H, t, J = 3Hz, H-4), 3.81 (6H, s, OCH_3), 4.67 (2H, t, J = 3Hz, H-1), 6.70 and 6.77 (2H, AB doublets, Ar-H).

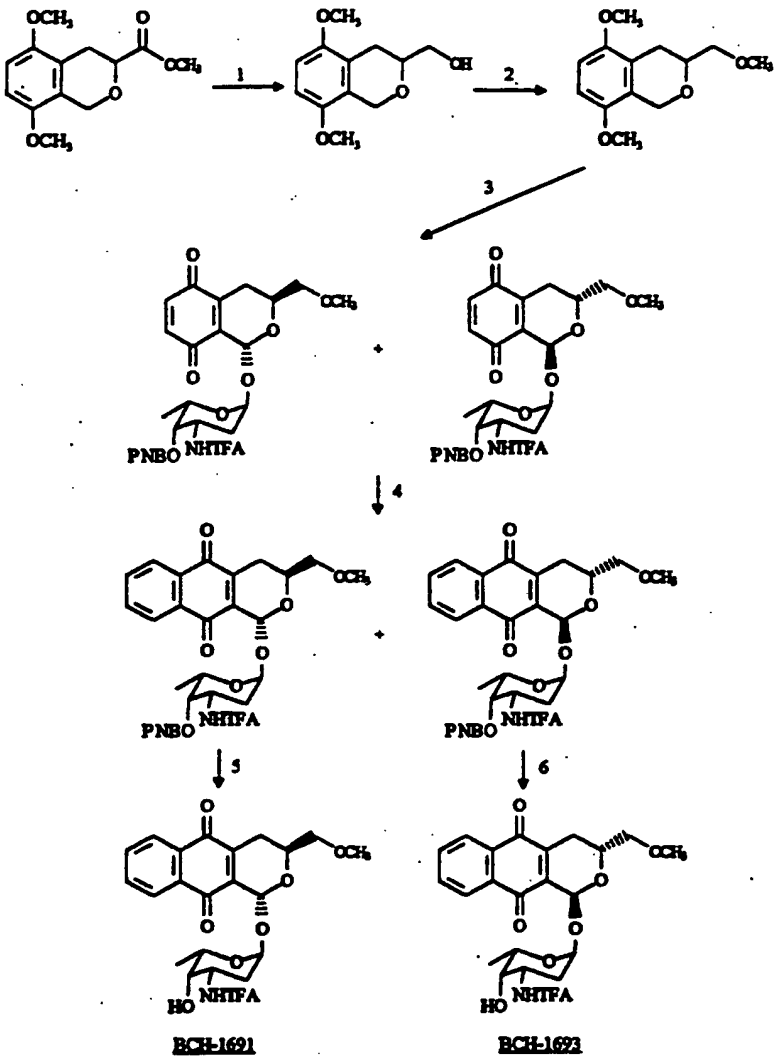
Step 3: **3,3 bis (methoxycarbonyl)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c] pyran**

To a solution of 5,8-dioxo-3,3 bis (methoxycarbonyl)-5,8-dihydroisochroman (50 mg; 0.17 mmol) in toluene (4 ml) at room temperature was added 1-acetoxy-1,3 butadiene (113 µl; 1 mmol). The resulting mixture was stirred at room temperature for 24 hours. Air was then bubbled through for 30 minutes and the mixture was concentrated to a volume of ~1 ml and applied to silica gel column. Elution with 30% ethyl acetate in hexane afforded pure title compound (20 mg; 34%) as a yellow solid; m.p.: 210-222°C (dec):

^{1}H NMR (250 MHz, $CDCl_3$) δ: 3.22 (2H, t, J = 2.5 Hz, H-4), 3.84 (6H, s, CO_2CH_3), 4.86 (2H, t, J = 2.5 Hz, H-1), 7.75 (2H, m, Ar-H), 8.10 (2H, m, Ar-H).

IR (film): 2963, 1743, 1662, 1641, 1591, 1438, 1288, 1175, 1055, 791 and 692 cm^{-1}.

Example 26: **Preparation of (1'S, 1R, 3S) and (1'S, 1S, 3R)-5,10-dioxo-3-methoxymethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran (BCH-1691) and BCH-1693)**



Step 1: **5,8-dimethoxy-3-hydroxymethyl-isochroman**

To a solution of 5,8-dimethoxy-3-methoxycarbonyl-isochroman (310 mg; 1.23 mmol) in 5 ml of tetrahydrofuran at 0°C was added lithium aluminum hydride (47 mg; 1.23 mmol). The mixture was stirred at 0°C for 15 minutes and was quenched with 1 N HCl. The product was extracted with ether and the combined organic layers were washed with brine and dried over $MgSO_4$ affording crude title alcohol (246 mg; 90%) used as such for subsequent steps:

^{1}H NMR (250 MHz, $CDCl_3$) δ: 2.42 (1H, m, H-4 ax), 2.55-2.75 (2H, m, H-4 eq and -OH), 3.60-3.90 (2H, m, CH_2-OH), 3.76 (3H, s, $-OCH_3$), 3.77 (3H, s, $-OCH_3$), 4.62 (1H, br d, J = 16.0 Hz, H-1), 4.97 (1H, d, J = 16.0 Hz, H-1), 6.61 and 6.65 (2H, AB doublets, ArH).

Step 2: 5,8-dimethoxy-3-methoxymethylisochroman

To a suspension of sodium hydride (70 mg of 60% in oil; 1.78 mmol) in tetrahydrofuran (3 ml) was added a solution of 5,8-dimethoxy-3-hydroxymethyl-isochroman (330 mg; 1.48 mmol) in 7 ml of tetrahydrofuran. The resulting mixture was stirred at room temperature until H_2 evolution ceased (~15 minutes) and iodomethane (500 µl; 5 eq) was added. The mixture was then stirred at room temperature for 30 minutes. Since the reaction was not complete, another equivalent of sodium hydride was added along with 20 mg of cesium carbonate. The mixture was stirred for 15 minutes and was quenched with saturated ammonium chloride solution and extracted with dichloromethane. The combined organic layers were washed with brine and dried over $MgSO_4$. The crude was purified by column chromatography on silica gel using 25% ethyl acetate in hexane to afford the title compound (301 mg; 86%):
^{1}H NMR (250 MHz, $CDCl_3$) δ: 2.45 (1H, br dd, J = 11.0 and 17 Hz, H-4 ax), 2.69 (1H, dm, J = 17.0 Hz, H-4 eq), 3.44 (3H, s, CH_2-O-CH_3), 3.55 (2H, d, J = 5.5 Hz, -CH_2-O), 3.75 (3H, s, OCH_3), 3.77 (3H, s, OCH_3), 4.63 (1H, br d, J = 16.0 Hz, H-1), 4.97 (1H, d, J = 16.0 Hz, H-1), 6.61 and 6.64 (2H, AB doublets, Ar-H).

Step 3: (1'S, 1R, 3S)-5,8-dioxo-3-methoxymethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexo-pyranose)-5,8-dihydroisochroman and its (1'S, 1S, 3R) diastereomer

To a solution of 5,8-dimethoxy-3-methoxymethyl-isochroman (280 mg; 1.18 mmol) in 16 ml of dichloromethane were added 2,3,6-trideoxy-3-trifluoroacetamido-4-O-p-nitrobenzoyl-α-L-lyxohexopyranose (555 mg; 1.42 mmol), 4Å molecular sieves (500 mg) and 2,3 dichloro-5,6-dicyanobenzoquinone (360 mg; 1.6 mmol). The dark green reaction mixture was stirred at room temperature for 14 hours. It was quenched with saturated $NaHCO_3$ solution and extracted with dichloromethane. The combined organic layers were washed with saturated $NaHCO_3$, brine and were dried over Na_2SO_4 affording, after evaporation, 671 mg of a crude adduct which was dissolved in acetonitrile (20 ml) at 0°C. A solution of ceric ammonium nitrate (3.3 g; 6 mmol) in 10 ml of water was treated by portions with solid sodium bicarbonate (886 mg). The resulting yellow solution was added dropwise to the isochroman solution. After the addition, the mixture was stirred at 0°C for 20 minutes, quenched with saturated $NaHCO_3$ solution and extracted with dichloromethane. The combined organic layers were washed with brine and dried over Na_2SO_4 to afford after evaporation a crude quinone which was recrystallized from dichloromethane:pentane yielding 225 mg of a diastereomeric quinone mixture favoring the title compound (2:1):
^{1}H NMR (250 MHz, $CDCl_3$): 1.20 (3H, t, J = 6.5 Hz, H-6'), 1.90-2.70 (4H, m, H-2' and H-4), 3.41 (3H, s, $-OCH_3$), 3.35-3.65 (3H, m, CH_2-OCH_3 and H-3'), 4.15-4.70 (2H, m, H-3 and H-5'), 5.44 (1H,

br s, H-1'), 5.60 (1H, br s, H-4'), 5.78 (1H, s, H-1), 6.30 (1H, m, NH), 6.65-6.90 (2H, m, Ar-H), 8.30 (4H, m, PNB): signals for minor (1'S, 1S, 3R) isomer are δ: 1.30 (3H, d, J = 6.5 Hz, H-6'), 1.90-2.70 (4H, m, H-2' and H-4), 3.43 (3H, s, $-OCH_3$), 3.35-3.65 (3H, m, CH_2-O-CH_3 and H-3'), 4.15-4.70 (2H, m, H-3 and H-5'), 5.40 (1H, br s, H-1'), 5.59 (1H, br s, H-4'), 5.91 (1H, s, H-1), 6.40 (1H, m, NH), 6.65-6.90 (2H, m, Ar-H), 8.30 (2H, m, Ar-H).

Step 4: **(1'S, 1R, 3S)-5,10-dioxo-3-methoxymethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexo-pyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran**

To a solution of the quinone mixture from step 3 of this example, (100 mg; 0.17 mmol) in 6 ml of toluene at room temperature was added 1-acetoxy-1,3-butadiene (113 µl; 1 mmol). The rest of the procedure is identical to step 2, example 5, affording the title compound (42 mg; 40%):
^1H NMR (CD_2Cl_2, 250 MHz) δ: 1.17 (3H, d, J = 6.5 Hz, H-6'), 1.90-2.20 (2H, m, H-2'), 2.37 (1H, dd, J = 11.5 and 19.5 Hz, H-4 ax), 2.70 (1H, dd, J = 3.5 and 19.5 Hz, H-4 eq), 3.38 (3H, s, O-CH_3), 3.55 (2H, m, -CH_2-OCH_3), 4.25-4.70 (3H, m, H-3, H-3' and H-5'), 5.41 (1H, br s, H-1'), 5.65 (1H, br s, H-4'), 5.90 (1H, s, H-1), 6.44 (1H, br d, J = 7 Hz, N-H), 7.75 (2H, m, Ar-H), 8.05 (2H, m, Ar-H), 8.27 (4H, m, PNB).
The second diastereomer:
(1'S, 1S, 3R)-5,10-dioxo-3-methoxymethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexo-pyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c] pyran was obtained in 19% yield and had:
^1H NMR (250 MHz, CD_2Cl_2) δ: 1.30 (3H, d, J = 6.5 Hz, H-6'), 1.90-2.30 (2H, m, H-2'), 2.47 (1H, dd, J = 11 and 19.5 Hz, H-4 ax), 2.71 (1H, dd, J = 4 and 19.5 Hz, H-4 eq), 3.89 (3H, s, $-OCH_3$), 3.57 (2H, d, J = 5 Hz, CH_2-OCH_3), 4.27 (1H, m, H-3), 4.52 (1H, m, H-3'), 4.75 (1H, q, J = 6.5 Hz, H-5'), 5.41 (1H br s, H-1'), 5.56 (1H, br s, H-4'), 6.03 (1H, s, H-1), 6.46 (1H, br d, J = 7.5 Hz, NH), 7.75 (2H, m, Ar-H), 8.07 (2H, m, Ar-H), 8.28 (4H, m, PNB).

Step 5: **(1'S, 1R, 3S)-5,10-dioxo-3-methoxymethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran (BCH-1691)**

To a solution of (1'S, 1R, 3S)-5,10-dioxo-3-methoxymethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitro-benzoyl-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-C] pyran (19 mg; .029 mmol) in methanol (.4 ml) and tetrahydrofuran (1.5 ml) at 0°C was added .86 µl (.1 eq) of a 4.37 M solution of sodium methoxyde in methanol. The resulting mixture was stirred at 0°C for 20 minutes and was quenched with saturated NH_4Cl. Extraction with dichloromethane followed by washing of the combined organic layers with brine and drying with Na_2SO_4 furnished a crude product which was purified by column chromatography on silica gel using 5-10% acetone in benzene as eluent yielding the

title compound (14 mg; 96%) which was recrystallized from dichloromethane:ether:pentane to give yellow crystals: M.P.: 140-159°C; IR (neat): 3500, 3422, 3320, 2938, 1715, 1667, 1597, 1295, 1178 and 980 cm^{-1}:

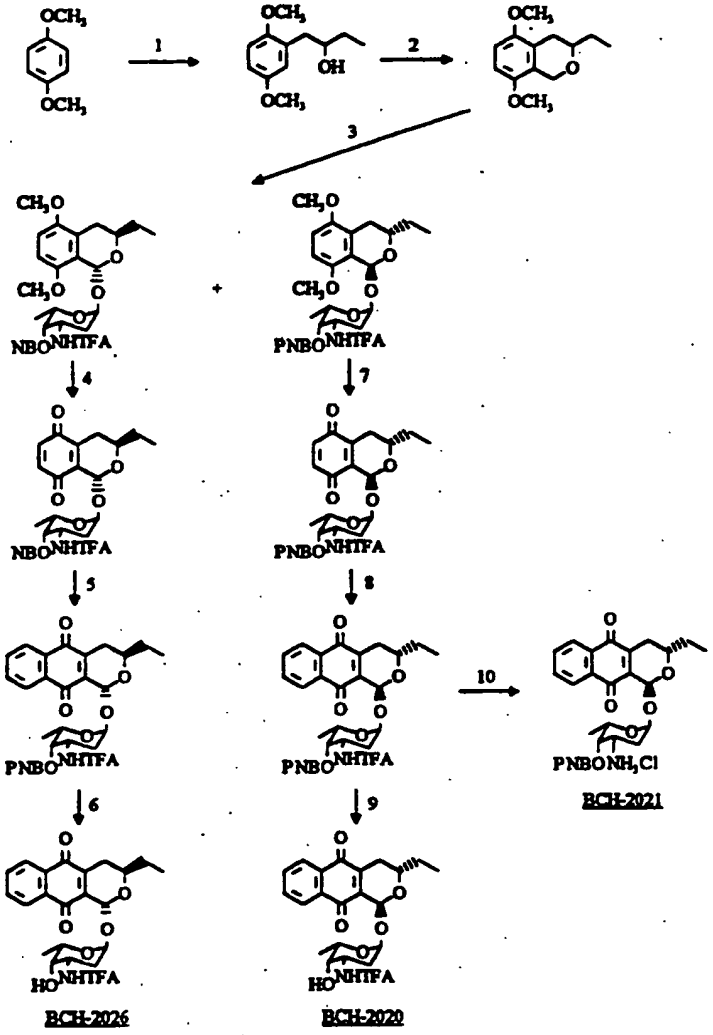
^1H NMR (250 MHz, CD_2Cl_2) δ: 1.21 (3H, d, J = 7.6 Hz, H-6'), 1.52 (1H, br s , O-H), 1.70-2.20 (2H, m, H-2'), 2.35 (1H, dd, J = 11.7 and 19.3 Hz, H-4 ax), 2.68 (1H, dd, J = 3.4 and 19.3 Hz, H-4 eq), 3.56 (3H, s, OCH_3), 3.52 (2H, d, J = 4.8 Hz, CH_2-OCH_3), 3.58 (1H, br s, H-4'), 4.15-4.40 (3H, m, H-3, H-3', H-5'), 5.46 (1H, br s, H-1'), 5.83 (1H, s, H-1), 6.73 (1H, br d, J = 7 Hz, N-H), 7.75 (2H, m, Ar-H), 8.05 (2H, m, Ar-H).

Step 6: (1'S, 1S, 3R)-5,10-dioxo-3-methoxymethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho [2,3-c] pyran (BCH-1693)

The starting protected alcohol from step 4 of this example (18 mg; 0.028 mmol) in .4 ml methanol and 1.5 ml of tetrahydrofuran was treated with .83 µl of a 4.37 M solution of sodium methoxide in methanol following the procedure from step 5 herein to afford the title compound (12.5 mg; 90%): m.p.: 92-102° C; IR (neat): 3485, 3424, 3323, 2937, 1715, 1666, 1595, 1296, 1175, 1117, 980 cm^{-1}.

^1H NMR (CD_2Cl_2, 250 MHz) δ: 1.35 (3H, d, J = 6.5 Hz, H-6'), 1.85 (2H, m, H-2'), 2.01 (1H, br d, J = 7 Hz, O-H), 2.46 (1H, dd, J = 11.5 and 20 Hz, H-4 ax), 2.69 (1H, dd, J = 3.7 and 20 Hz, H-4 eq), 3.36 (3H, s, OCH_3), 3.54 (2H, d, J = 4.7 Hz, CH_2-OCH_3), 3.60 (1H, m, H-4'), 4.15-4.40 (2H, m, H-3' and H-3), 4.55 (1H, q, J = 6.5 Hz, H-5'), 5.39 (1H, br s, H-1'), 5.98 (1H, s, H-1), 6.78 (1H, br d, J = 7 Hz, -NH), 7.75 (2H, m, Ar-H), 8.05 (2H, m, Ar-H).

Example 27: **Preparation of (1'S,1R,3S) and 1'S,1S,3S)-5,10-dioxo-3-ethyl-1-(2',3',6'-trideoxy-3'trifluoroacetamido-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran: (BCH-2026) and BCH-2020) and (1'S,1S,3S)-5,10-dioxo-3-ethyl-1-(2',3',6'-trideoxy-3'-amino-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran hydrochloride: (BCH-2021)**



Step 1: **1-(2,5-dimethoxyphenyl)-2-butanol**

Under argon atmosphere, 1,4-dimethoxybenzene 10.0 g (72.37 mmol) was dissolved in dry THF and this solution was cooled to 0°C. n-BuLi (2.5 M/hexanes) 28.8 ml (72.37 mmol) was then added and the reaction mixture was warmed up to room temperature and stirring was left for 4 hours. After 4 hours, the reaction was cooled to -78°C and 1,2-epoxybutane 5.2 g (72.37 mmol) was added followed by 10.2 g (72.37 mmol) of boron trifluoro etherate. Stirring was then continued for a period of 1 hour. The reaction mixture was then quenched by pouring it into 125 ml of aqueous NH_4Cl. Extractions of the

aqueous layer were done using CH_2Cl_2. The combined organic layers were dried over Na_2SO_4, filtered and the solvent was removed. The crude material was purified by flash chromatography with hexanes-ethyl acetate (9:1) then (8:2) as the eluent. The isolated titled compound was a white solid (11.4 g, 75%).

NMR ^1H (250 MHz) ($CDCl_3$; ppm): 6.75 (3H, m, aromatics), 3.79 (3H, s, OCH_3), 3.77 (1H, m, $H_{2'}$), 3.76 (3H, s, OCH_3), 2.85 (1H, dd, J_1 = 3.8 Hz, J_2 = 13.5 Hz, $H_{1'a}$), 2.65 (1H, dd, J_1 = 8.1 Hz, J_2 = 13.5 Hz, H_{1b}), 2.16 (1H, d, J = 3.7 Hz, OH), 1.52 (2H, m, $H_{3'}$) 0.99 (3H, dd, $J_1 = J_2$ = 7.4 Hz, $-CH_3$).

Step 2: 5,8-dimethoxy-3-ethyl-isochroman

Under argon atmosphere, the starting material from step 1 of this example, 5.00 g (23.78 mmol) was dissolved in 100 ml of dry ether. Dimethoxy methane 3.0 ml (33.90 mmol) and boron trifluoro etherate 9.0 ml (71.35 mmol) were then added and stirring was left overnight. The reaction was then quenched using aqueous $NaHCO_3$. Extractions were done using ether and the combined organic extracts were dried over Na_2SO_4, filtered and the solvent was removed. The isolated residue was then purified by flash chromatography; hexanes-ethyl acetate (8:2) was used as the eluent. The desired titled compound was isolated as a white solid (4.9 g; 92%).

NMR ^1H (250 MHz) ($CDCl_3$; ppm): 6.63 (2H, d, J = 3.4 Hz, aromatics), 4.93 (1H, d, J = 15.9 Hz, H_{1a}), 4.57 (1H, d, J = 15.9 Hz, H_{1b}), 3.78 (3H, s, OCH_3), 3.76 (3H, s, OCH_3), 3.47 (1H, m, H_3), 2.74 (1H, ddd, H_{4a}), 2.38 (1H, dd, H_{4b}), 1.68 (2H, m, $-CH_2$- side chain) 1.03 (3H, dd, $J_1 = J_2$ = 7.4 Hz, $-CH_3$).

Step 3: (1'S, 1R, 3R)-5,8-dimethoxy-3-ethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-isochroman

Application of the first part of the procedure described in step 3, example 26, on the isochroman precursor from step 2 herein resulted with the titled compound as a yellow solid; 62%.

NMR ^1H (250 MHz) (C_6D_6; ppm): 7.72 (4H, m, aromatics), 6.48 (2H, d, J = 4.7 Hz, aromatics), 6.17 (1H, s, H_1), 5.95 (1H, m, NH), 5.67 (1H, d, $H_{4'}$), 5.29 (1H, d, $H_{1'}$), 4.67 (1H, m, $H_{3'}$), 4.26 (1H, q, $H_{5'}$), 4.20 (1H, m, H_3), 3.49 (3H, s, OCH_3), 3.40 (3H, s, OCH_3), 3.01 (1H, dd, H_{4a}), 2.52 (1H, dd, H_{4b}), 1.90 (1H, m, $-CH_2$ side chain), 1.75 (1H, m, $-CH_2$- side chain), 1.61 (2H, m, $-CH_2$- sugar), 1.06 (3H, d, $-CH_3$ sugar), 1.03 (3H, m, CH_3 side chain).

IR (film) (cm^{-1}): 3316 (NH), 2933 (CH aliphatic), 1733 (C=O), 1707 (C=O), 1603 (C=C), 1532 (C-N), 1259 and 1175 (C-O).

Step 4: (1'S, 1R, 3R)-5,8-dioxo-3-ethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-isochroman

Application of the second part of the procedure (CAN) described in step 3, example 26, on the glycosylated isochroman precursor from the previous step resulted in an 87% yield of the titled compound.

NMR ^1H (250 MHz) (C_6D_6; ppm): 7.80 (4H, m, aromatics), 6.92 (1H, s_{broad}, NH), 6.08 (2H, m, quinone ring), 5.72 (1H, s, H_1), 5.54 (1H, s, $H_{4'}$), 5.53 (1H, s, $H_{1'}$), 4.74 (1H, m, $H_{3'}$), 4.36 (1H, m, $H_{5'}$), 3.68 (1H, m, H_3), 2.28 (1H, dd, J_1 = 3.2 Hz, J_2 = 19.3 Hz, H_{4a}), 1.88 (2H, m, -CH_2- sugar), 1.80 (1H, dd, H_{4b}), 1.49 (2H, m, -CH_2- side chain), 1.15 (3H, d, J = 6.5 Hz, CH_3 sugar), 0.89 (3H, dd, $J_1 = J_2$ = 7.4 Hz, -CH_3 side chain).

Step 5: (1'S, 1R, 3R)-5,10-dioxo-3-ethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c] pyran

The titled compound was obtained via Diels-Alder cycloaddition between 1-acetoxylbutadiene and the quinone from step 4 from this example using the procedure described in step 4 from example 26.

NMR ^1H (250 MHz) (CD_2Cl_2; ppm): 8.28 (4H, d, J = 4.3 Hz, aromatics), 8.05 (2H, m, aromatics), 7.73 (2H, m, aromatics), 6.31 (1H, d, NH), 5.87 (1H, s, H_1), 5.67 (1H, s, $H_{4'}$), 5.42 (1H, s, $H_{1'}$), 4.58 (1H, m, $H_{3'}$), 4.42 (1H, q, J = 6.3 Hz, $H_{5'}$), 4.05 (1H, m, H_3), 2.78 (1H, dd, J_1 = 3.4 Hz, J_2 = 19.5 Hz, H_{4a}), 2.24 (1H, dd, J_1 = 11.3 Hz, J_2 = 19.0 Hz, H_{4b}), 2.05 (2H, m, -CH_2- sugar), 1.70 (2H, m, -CH_2- side chain), 1.18 (3H, d, J = 6.5 Hz, -CH_3 sugar), 1.05 (3H, dd, $J_1 = J_2$ = 7.4 Hz, -CH_3 side chain).

IR (film) (cm^{-1}): 3332 (NH), 2955 and 2929 (CH aliphatic), 1740 (C=O), 1669 (C=C), 1529 (C-N), 1279 and 1180 (C-O).

Step 6: (1'S, 1R, 3R)-5,10-dioxo-3-ethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c] pyran (BCH-2026)

The titled compound was in 64% yield from the glycoside of step 5 of this example as per procedure described in step 5 of example 26.

NMR ^1H (250 MHz) (CD_2Cl_2; ppm): 8.03 (2H, m, aromatics), 7.71 (2H, m, aromatics), 6.77 (1H, d, NH), 5.81 (1H, s, H_1), 5.50 (1H, d, J = 2.8 Hz, $H_{1'}$), 4.26 (1H, m, $H_{3'}$), 4.22 (1H, m, $H_{5'}$), 4.05 (1H, m, H_3), 3.58 (1H, d, J = 2.2 Hz, $H_{4'}$), 2.76 (1H, dd, J_1 = 3.5 Hz, J_2 = 19.5 Hz, H_{4a}), 2.21 (1H, ddd, J_1 = 0.9 Hz, J_2 = 11.0 Hz, J_3 = 19.5 Hz, H_{4b}), 2.07 (1H, $s_{(broad)}$, OH), 1.83 (2H, m, -CH_2-sugar), 1.67 (2H, m, -CH_2- side chain), 1.23 (3H, d, J = 6.6 Hz, -CH_3 sugar), 1.02 (3H, dd, $J_1 = J_2$ = 7.5 Hz, -CH_3 side chain).

Step 7: (1'S, 1S, 3S)-5,8-dioxo-3-ethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexo-pyranose)-5,8-dihydro-isochroman

To a solution of (1'S, 1S, 3S)-5,8-dimethoxy-3-ethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitro-benzoyl-L-lyxohexopyranose)-isochroman (372 mg; 0.60 mmol) in acetonitrile (12 ml) was added a solution of CAN prepared by dissolving ceric ammonium nitrate (2.0 g; 3.6 mmol) in 6 ml of water and then slowly adding solid sodium bicarbonate (531 mg). The resulting mixture was stirred at 0°C for 20 minutes and was then quenched with saturated bicarbonate solution. The product was extracted with dichloromethane and the combined organic layers were washed with brine and dried over Na_2SO_4 to give after evaporation the crude title compound:
(360 mg; 100%): ^1H NMR (250 MHz; $CDCl_3$) δ: 1.02 (3H, t, J = 7.5 Hz, CH_2-CH_3), 1.29 (3H, d, J = 6.5 Hz, H-6'), 1.65 (2H, m, CH_2-CH_3), 1.80-2.30 (3H, m, H-2' and H-4 ax), 2.60 (1H, dd, J = 3.5 and 19.5 Hz, H-4 eq), 3.89 (1H, m, H-3), 4.50-4.80 (2H, m, H-3' and H-5'), 5.41 (1H, br s, H-1') 5.55 (1H, br s, H-4'), 5.87 (1H, s, H-1), 6.58 (1H, br d, J = 7.5 Hz, NH), 6.75 and 6.81 (2H, AB doublets, ArH), 8.28 (4H, br s, PNB).

Step 8: (1'S, 1S, 3S)-5,10-dioxo-3-ethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexo-pyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran

Using the procedure described in step 4, example 26, the starting quinone from step 7 herein (330 mg; 0.57 mmol) was treated with 1-acetoxy-1,3-butadiene (379 µl; 3.4 mmol) in 20 ml of toluene to afford after chromatography the title compound (165 mg; 46%).
^1H NMR (250 MHz, CD_2Cl_2) δ: 1.03 (3H, d, J = 7.5 Hz, CH_2-CH_3), 1.30 (3H, d, J = 6.5 Hz, H-6'), 1.68 (2H, qn, J = 7.5 Hz, CH_2-CH_3), 1.95 (1H, m, H-2 eq), 2.12 (1H, td, J = 13 and 3.5 Hz, H-2' ax), 2.29 (1H, dd, J = 11.5 and 19.5 Hz, H-4 ax), 2.76 (1H, dd, J = 3.5 and 19.5 Hz, H-4 eq), 3.97 (1H, m, H-3), 4.55 (1H, m, H-3'), 4.78 (1H, q, J = 6.5 Hz, H-5'), 5.41 (1H, br s, H-1'), 5.57 (1H, d, J = 6.5 Hz, H-4'), 6.01 (1H, s, H-1), 6.51 (1H, br d, J = 7.5 Hz, -NH), 7.75 (2H, m, ArH), 8.07 (2H, m, Ar-H), 8.27 (4H, s, PNB).

Step 9: (1'S, 1S, 3S)-5,10-dioxo-3-ethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran (BCH-2020)

The starting protected alcohol from step 8 herein (20 mg; .032 mmol) was treated with sodium methoxide in methanol (4.37 M, 1 µl) in 1 ml of tetrahydrofuran and .3 ml of methanol according to the procedure described in step 5, example 26, affording after chromatography (15% acetone in benzene) the title compound (11.5 mg, 75%), M.P. 208-211°C.
IR (neat): 3540, 3292, 2978, 1705, 1666, 1556, 1295, 1187, 1165 and 990 cm^{-1}.

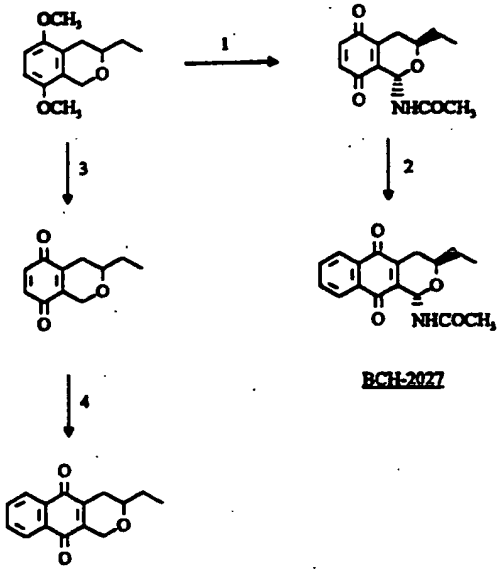
^{1}H NMR (250 MHz, CD_2Cl_2): 1.00 (3H, t, J = 7.5 Hz, CH_2-CH_3), 1.35 (3H, d, J = 6.5 Hz, H-6'), 1.66 (2H, qn, J = 7.5 Hz, CH_2-CH_3), 1.80-2.20 (3H, m, H-2' and O-H), 2.27 (1H, dd, J = 11.0 and 19.5 Hz, H-4 ax), 2.75 (1H, dd, J = 3.5 and 19.5 Hz, H-4 eq), 3.61 (1H, br s, H-4'), 3.96 (1H, m, H-3), 4.25 (1H, m, H-3'), 4.58 (1H, q, J = 6.5 Hz, H-5'), 5.40 (1H, t, J = 2.0 Hz, H-1'), 5.97 (1H, s, H-1), 6.77 (1H, m, N-H), 7.75 (2H, m, Ar-H), 8.05 (2H, m, Ar-H).

Step 10: (1'S, 1S, 3S)-5,10-dioxo-3-ethyl-1-(2',3',6'-trideoxy-3'-amino-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran (BCH-2021)

To a solution of the starting protected amino-alcohol from step 9 herein (43 mg; 0.07 mmol) in acetonitrile (6 ml) was added dropwise .1 N sodium hydroxide (3 ml). The mixture was stirred at 0°C for 30 minutes and an extra 1 ml of sodium hydroxide solution was added and the resulting mixture was stirred for 1 hour at 0°C. It was then quenched with .1 N HCl and extracted with dichloromethane. The water layer was neutralized to pH ~7 by addition of dilute sodium hydroxide. It was then extracted with dichloromethane. To the organic extract were added 1.5 ml of .1 N HCl, 5 ml of methanol and 25 ml of ether and the mixture was evaporated partially in order to induce crystallization. Since no crystallization occured, the solvents were evaporated completely and the residue was dissolved in methanol (1 ml) and 200 µl of .1 N HCl were added followed by 25 ml of ether. A precipitate formed which was filtered and washed with ether yielding the crude title compound (3.8 mg; 13%).

^{1}H NMR (250 MHz, DMSO-D6), δ: 0.97 (3H, t, J = 7.0 Hz, CH_2-CH_3), 1.23 (3H, d, J = 6.5 Hz, H-6'), 1.50-1.80 (3H, m, CH_2-CH_3 and H-2' eq), 1.97 (1H, m, H-2' ax), 2.23 (1H, dd, J = 11.0 and 19.5 Hz, H-4 ax), 2.72 (1H, dd, J = 3.0 and 19.5 Hz, H-4 eq), 3.63 (1H, m, H-4'), 3.87 (1H, m, H-3), 4.33 (1H, m, H-5'), 5.29 (1H, br s, H-1'), 5.53 (1H, m, H-3'), 5.82 (1H, s, H-1), 7.85 (2H, m, Ar-H), 8.05 (5H, m, Ar-H and N-H).

Example 28: **Preparation of trans-5,10 dioxo-1-acetamido-3-ethyl-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran: (BCH-2027) and 3-ethyl-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran: (BCH-2154)**



BCH-2027

BCH-2154

Step 1: **(trans)-1-acetamido-5,8-dioxo-3-ethyl-5,8-dihydro-isochroman**

To a solution of 5,8-dimethoxy-3-ethyl-isochroman (1.0 g; 4.5 mmol) in dichloromethane (30 ml) at room temperature were added methanol (211 µl; 5.4 mmol), 4Å molecular sieves (2 g) and 2,3-dichloro-5,6-dicyano-benzoquinone (1.21 g; 5.4 mmol). The resulting dark mixture was stirred for 5 hours and was then quenched with saturated $NaHCO_3$ solution. It was extracted with dichloromethane and the combined organic layers were washed with bicarbonate, brine and then dried over Na_2SO_4 affording after evaporation 1.0 g of crude adduct of which 300 mg (1.19 mmol assumed) were placed in a pear-shaped flask along with acetamide (70 mg; 1.19 mmol). The solid mixture was then heated to 130 °C for 30 minutes. It was then cooled to room temperature and dichloromethane was added followed by pentane yielding a precipitate (160 mg) of which 120 mg (.43 mmol assumed) was dissolved in acetonitrile (15 ml) and treated with a solution of CAN prepared by slowly dissolving sodium bicarbonate (384 mg) in water (5 ml) containing cerium ammonium nitrate (1.46 g; 2.5 mmol). The resulting mixture was stirred at room temperature for 15 minutes and was quenched with saturated $NaHCO_3$ solution followed by extraction with dichloromethane. The combined organic extracts were washed with brine and dried over Na_2SO_4 to afford the titled compound as a yellow solid (125 mg; 42% overall).

^1H NMR (250 MHz, $CDCl_3$) δ: 0.99 (3H, t, J = 7.5 Hz, $C\underline{H}_3$-CH_2), 1.65 (2H, m, -$C\underline{H}_2$-CH_3), 2.02 (3H, s, -CH_3), 2.20 (1H, m, H-4 ax), 2.60 (1H, dd, J = 3.5 and 19.5 Hz, H-4 eq), 3.70 (1H, m, H-3), 6.12 (2H, br s, H-1 and N-H), 6.73 and 6.78 (2H, AB system, Ar-H).

Step 2: Trans-5,10-dioxo-1-acetamido-3-ethyl-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran

To a solution of the starting quinone from step 1 herein (56 mg; .22 mmol) in toluene (50 ml) was added 1-acetoxy-1,3-butadiene (30 µl; 11 eq). The mixture was stirred overnight at room temperature and was then concentrated and applied to a column of silica gel using 1-15% acetone in benzene to elute the product which was then recrystallized from dichloromethane:pentane affording the title compound as a yellow solid (10 mg; 15%).

^{1}H NMR (250 MHz, DMSO-D6), δ: 0.90 (3H, t, J = 7.5 Hz, CH_3-CH_2), 1.58 (2H, m, CH_2-CH_3), 1.82 (3H, s, CH_3-C=O), 2.20 (1H, m, H-4 ax), 2.64 (1H, br d, J = 16.0 Hz, H-4 eq), 3.71 (1H, m, H-3), 6.17 (1H, d, J = 8.0 Hz, H-1), 7.88 (2H, m, Ar-H), 8.01 (2H, m, Ar-H), 8.78 (1H, d, J = 8.0 Hz, N-H).

Step 3: 5,8-dioxo-3-ethyl-5,8-dihydro-isochroman

To a solution of 3-ethyl-5,8-dimethoxy-isochroman (300 mg; 1.35 mmol) in acetonitrile (10 ml) at room temperature was added dropwise a solution of CAN (prepared by dissolving ceric ammonium nitrate (2.22 g; 4.0 mmol) in water (5 ml)). The resulting mixture was quenched with saturated bicarbonate solution and extracted with dichloromethane. The combined organic layers were washed with brine and dried over Na_2SO_4 affording the crude title compound (251 mg; 97%) which was used as such for subsequent steps.

^{1}H NMR (250 MHz, $CDCl_3$) δ: 0.97 (3H, t, J = 7.5 Hz, CH_2-CH_3), 1.60 (2H, m, -CH_2-CH_3), 2.10 (1H, m, H-4), 2.52 (1H, m, H-4), 3.35 (1H, m, H-3), 4.30 (1H, m, H-1), 4.62 (1H, br d, J = 16 Hz, H-1), 6.68 (2H, m, Ar-H).

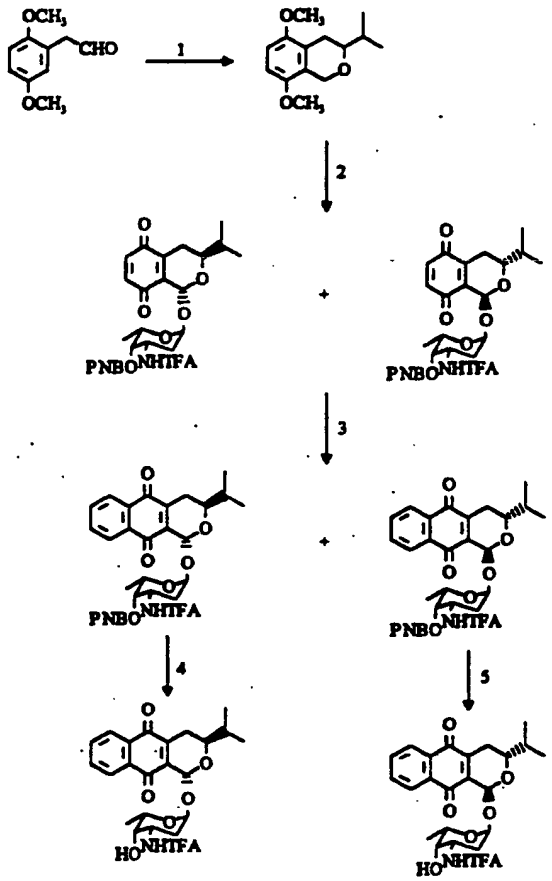
Step 4: 3-ethyl-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c] pyran

Following the procedure described in step 4, example 26, the starting quinone from step 3 herein (250 mg; 1.30 mmol) and 1-acetoxy-1,3-butadiene (876 µl; 7.8 mmol) were reacted in toluene (10 ml) to yield after chromatography using 2% ethyl acetate in toluene the title compound (62 mg; 20%) along with mixed fractions containing a lot of desired titled product (230 mg), M.P.: 98-101°C.

IR (neat): 2963, 2938, 2876, 1658, 1636, 1593, 1337, 1299, 1176 and 698 cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$) δ: 1.04 (3H, t, J = 7.5 Hz, CH_3-), 1.70 (2H, m, CH_2-CH_3), 2.30 (1H, m, H-4 ax), 2.75 (1H, br d, J = 19.0 Hz, H-4 eq), 3.45 (1H, m, H-3), 4.50 (1H, dt, J = 4.0 and 18.5 Hz, H-1), 4.86 (1H, dd, J = 2.5 and 18.5 Hz, H-1), 7.72 (2H, m, Ar-H), 8.18 (2H, m, Ar-H).

Example 29: **Preparation of (1'S,1R,3S) and (1'S,1S,3R)-5,10-dioxo-3-isopropyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran: (BCH-2053) and (BCH-2052)**



Step 1: **3-isopropyl-5,8-dimethoxy-isochroman**

To a solution of the starting aldehyde (1.16 g; 6.44 mmol) in tetrahydrofuran (25 ml) at 0°C was added a solution of isopropyl magnesium chloride (2 M in THF; 6.4 ml; 12.88 mmol). The resulting mixture was stirred at 0°C for 1 hour and at room temperature for 30 minutes. It was then quenched with saturated ammonium chloride solution and extracted with ether. The combined organic layers were washed with brine and dried over $MgSO_4$ to yield a crude alcohol (1.29 g) which was dissolved in ether (40 ml). To this solution were added dimethoxymethane (777 µl; 8.55 mmol) and boron trifluoride-etherate (2.02 ml; 17.1 mmol). The resulting mixture was stirred at room temperature for 20 hours and was then quenched with saturated sodium bicarbonate solution. It was then extracted with ether and the combined organic layers were washed with brine and dried over $MgSO_4$. The crude product was then

purified by column chromatography on silica gel using 20-30% ethyl acetate in hexane as eluent to give the title compound (607 mg; 40% overall).

^{1}H NMR ($CDCl_3$) δ: 1.00 and 1.05 (6H, 2d, J= 7 Hz, -CH-($C\underline{H}_3$)$_2$), 1.84 (1H, sept., J = 7 Hz, C$\underline{H}$-(CH_3)$_2$), 2.42 (1H, dd, J = 11 and 17 Hz, H-4 ax), 2.74 (1H, dm, J = 17 Hz, H-4 eq), 3.22 (1H, m, H-3), 3.76 (3H, s, OCH_3), 3.79 (3H, s, OCH_3), 4.56 (1H, dm, J = 16 Hz, H-1), 4.95 (1H, d, J = 16 Hz, H-1), 6.63 (2H, AB system, Ar-H).

Step 2: **(1'S, 1R, 3S) and (1'S, 1S, 3R)-5,8-dioxo-3-isopropyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-5,8-dihydro-isochroman (40:60)**

Using the procedure described in step 3, example 26, the starting isochroman from step 1 herein (300 mg; 1.27 mmol) afforded a crude diastereomeric mixture of glycosidated isochromans (515 mg) which was reacted with CAN as described in step 3, example 26, to afford a diastereomeric title quinones mixture (450 mg; 59%) in a ratio of (40:60) favoring the 1'S, 1S, 3R isomer which were used as such for the next reactions.

For minor isomer: ^{1}H NMR (250 MHz, $CDCl_3$) δ: 0.90-1.40 (9H, m, H-6' and -CH(-$C\underline{H}_3$)$_2$), 1.70-2.35 (4H, m, H-2', H-4 ax and C$\underline{H}$-CH_3), 2.62 (1H, m, H-4 eq), 3.80 (1H, m, H-3), 4.42 (1H, q, J = 6.5 Hz, H-5'), 4.50-4.70 (1H, m, H-3'), 5.44 (1H, br s, H-1'), 5.63 (1H, br s, H-4'), 5.74 (1H, s, H-1), 6.32 (1H, m, N-H), 6.70-6.90 (2H, m, Ar-H), 8.30 (4H, m, PNB).

For major isomer: 0.90-1.40 (9H, m, H-6' and CH(-$C\underline{H}_3$)$_2$), 1.70-2.35 (4H, m, H-2', H-4 ax and C$\underline{H}$-CH_3), 2.62 (1H, m, H-4 eq), 3.69 (1H, m, H-3), 4.50-4.75 (2H, m, H-3' and H-5'), 5.42 (1H, br s, H-1'), 5.56 (1H, d, J = 3 Hz, H-4'), 5.88 (1H, s, H-1), 6.43 (1H, br d, J = 7.5 Hz, N-H), 6.70-6.90 (2H, m, Ar-H), 8.30 (4H, m, PNB).

Step 3: **(1'S, 1S, 3R)-5,10-dioxo-3-isopropyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexo-pyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran**

Using the procedure described in step 4, example 26, the starting quinone mixture from step 2 herein (100 mg; .167 mmol) was treated with 1-acetoxy-1,3-butadiene (112 µl; 1 mmol) in 5 ml of toluene to afford the title compound (34 mg pure + 9 mg of 1:1 mixture of diastereomers).

^{1}H NMR (250 MHz, CD_2Cl_2) δ: 1.01 and 1.04 (6H, 2d, J = 6.5 Hz, -CH-($C\underline{H}_3$)$_2$), 1.31 (3H, d, J = 6.5 Hz, H-6'), 1.70-2.02 (2H, m, H-2' and C$\underline{H}$-(CH_3)$_2$), 2.13 (1H, t d, J = 3.5 and 13 Hz, H-2'), 2.34 (1H, dd, J = 11.5 and 19.5 Hz, H-4 ax), 2.78 (1H, dd, J = 3.5 and 19.5 Hz, H-4 eq), 3.76 (1H, m, H-3), 4.55 (1H, m, H-3'), 4.80 (1H, q, J = 6.5 Hz, H-5'), 5.42 (1H, d, J = 2.5 Hz, H-1'), 5.58 (1H, d, J = 3 Hz, H-4'), 6.03 (1H, s, H-1), 6.52 (1H, br d, J = 7.5 Hz, -NH), 7.75 (2H, m, Ar-H), 8.05 (2H, m, Ar-H), 8.28 (4H, s, PNB).

The second diastereomer:

(1'S, 1R, 3S)-5,10-dioxo-3-isopropyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexo-pyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran, obtained in 16% yield, had ^{1}H NMR (250 MHz, CD_2Cl_2) δ: 0.90-1.10 (6H, m, CH-($C\underline{H}_3$)$_2$), 1.17 (3H, d, J = 6.5 Hz, H-6'), 1.70-2.40 (4H, m, H-2', C$\underline{H}$-(CH_3)$_2$) and H-4), 2.60-2.90 (1H, m, H-4), 3.87 (1H, m, H-3), 4.44 (1H, q, J = 6.5 Hz, H-5'), 4.58 (1H, m, H-3'), 5.42 (1H, br s, H-1'), 5.69 (1H, br s, H-4'), 5.89 (1H, s, H-1), 6.40 (1H, br d, J = 7.5 Hz, -NH), 7.75 (2H, m, Ar-H), 8.06 (2H, m, Ar-H), 8.28 (4H, m, PNB).

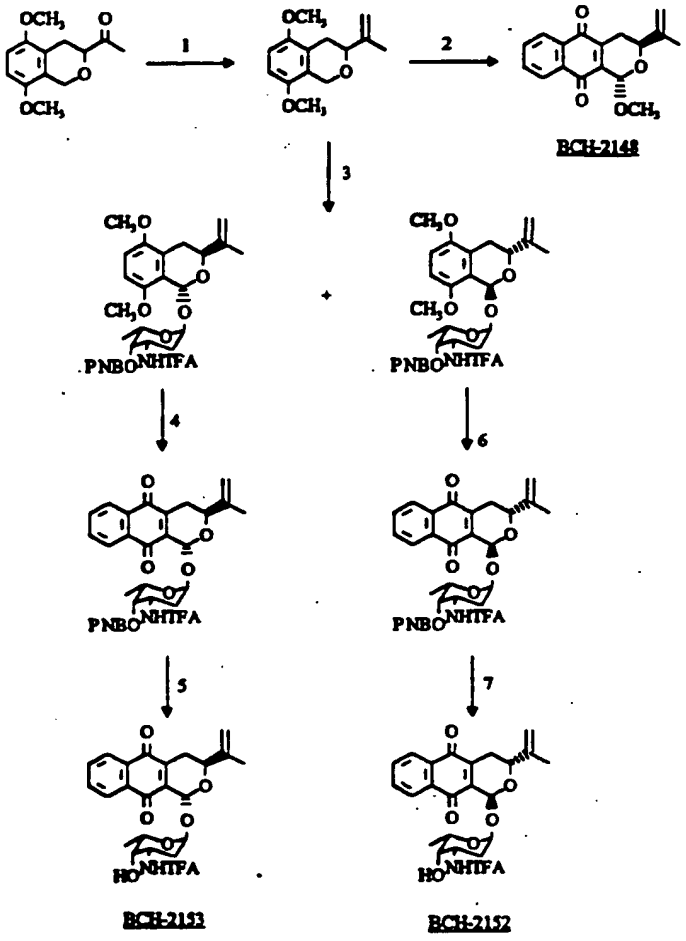
Step 4: (1'S, 1R, 3S)-5,10-dioxo-3-isopropyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran (BCH-2053)

Using the procedure described in step 5, example 26, the starting protected alcohol from step 3 herein (11 mg; .017 mmol) was treated with NaOMe/MeOH (4.37 M; 1 µl; .26 eq) to yield after column chromatography (7% acetone in benzene) the title compound (5 mg; 59%), M.P.: 180-185°C.
IR (neat): 3491, 3423, 3325, 2962, 2938, 1721, 1670, 1596, 1293, 1179, 982 cm^{-1}.
^{1}H NMR (250 MHz, CD_2Cl_2): 1.00 and 1.01 (6H, 2d, J = 6.5 Hz, -CH-($C\underline{H}_3$)$_2$), 1.22 (3H, d, J = 6.5 Hz, H-6'), 1.60-2.00 (4H, m, -C$\underline{H}$-(CH_3)$_2$, H-2' and OH), 2.27 (1H, br dd, J = 11.0 and 19.5 Hz, H-4 ax), 2.74 (1H, dd, J = 3.5 and 19.5 Hz, H-4 eq), 3.58 (1H, d, J = 2.5 Hz, H-4'), 3.85 (1H, m, H-3), 4.25 (2H, m, H-3' and H-5'), 5.52 (1H, d, J = 3.0 Hz, H-1'), 5.82 (1H, s, H-1), 6.75 (1H, m, NH), 7.74 (2H, m, Ar-H), 8.03 (2H, m, Ar-H).

Step 5: (1'S, 1S, 3R)-5,10-dioxo-3-isopropyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran (BCH-2052)

Using the procedure described in step 5, example 26, the starting protected alcohol from step 3 herein (32 mg; .0495 mmol) afforded after flash chromatography using 7% acetone in benzene as eluent, a gummy product which was dissolved in dichloromethane and precipitated with pentane yielding the title product (16 mg; 65%), M.P.: 212-213°C.
IR (neat): 3509, 3421, 3333, 2961, 2944, 1718, 1667, 1592, 1292, 1166 and 979 cm^{-1}.
^{1}H NMR (250 MHz, CD_2Cl_2): 0.98 and 1.00 (6H, 2d, J = 6.7 Hz, -CH($C\underline{H}_3$)$_2$), 1.36 (3H, d, J = 6.5 Hz, H-6'), 1.70-2.00 (4H, m, -C$\underline{H}$(CH_3)$_2$, H-2' and -OH), 2.32 (1H, dd, J = 11.5 and 19.5 Hz, H-4 ax), 2.76 (1H, dd, J = 3.5 and 19.5 Hz, H-4 eq), 3.61 (1H, br s, H-4'), 3.74 (1H, ddd, J = 3.5, 6.5 and 11.5 Hz, H-3), 4.24 (1H, m, H-3'), 4.59 (1H, q, J = 6.5 Hz H-5'), 5.39 (1H, t, J = 2.0 Hz, H-1'), 5.97 (1H, s, H-1), 6.77 (1H, m, NH), 7.72 (2H, m, Ar-H), 8.05 (2H, m, Ar-H).

Example 30: **Preparation of (1'S,1R,3S) and (1'S,1S,3R)-5,10-dioxo-3-isopropenyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran: (BCH-2153) and (BCH-2152) and trans-5,10-dioxo-3-isopropenyl-1-methoxy-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran: (BCH-2148)**



Step 1: **5,8-dimethoxy-3-isopropenyl-isochroman**

To a solution of methyltriphenylphosphonium bromide (2.26 g; 6.4 mmol) in ether (75 ml) at room temperature (not totally soluble) was added n-BuLi (2.5 M in hexanes; 2.03 ml; 5.1 mmol). The resulting mixture was stirred at room temperature for 1 hour. A solution of 5,8-dimethoxy-3-(1-acethyl)-isochroman (1.0 g; 4.2 mmol) was then added to the yellow-orange mixture and the resulting solution was stirred at room temperature for 3 hours. The mixture was then quenched with NH_4Cl (sat.) and extracted with ether. The combined organic layers were washed with brine and dried over Na_2SO_4. The crude mixture was then purified by column chromatography in silica gel using 25% ethyl acetate in hexane as eluent to afford the title compound (541 mg; 55%).

^{1}H NMR (250 MHz, $CDCl_3$) δ: 1.86 (3H, s, =C-CH_3), 2.58 (1H, br dd, J = 11 and 17 Hz, H-4 ax), 2.85 (1H, ddd, J = 1.5, 3.5 and 17 Hz, H-4 eq), 3.77 and 3.79 (6H, 2s, -O-CH_3), 4.00 (1H, dd, J = 3.5 and 11 Hz, H-3), 4.66 (1H, br d, J = 16 Hz, H-1), 4.93 (1H, br s, =CH_2), 4.99 (1H, d, J = 16Hz, H-1), 5.09 (1H, br s, =CH_2), 6.62 and 6.67 (2H, 2d (AB), J = 9 Hz, Ar-H).

Step 2: **(trans)-5,10-dioxo-3-isopropenyl-1-methoxy-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran (BCH-2148)**

Using the procedure described in step 3, example 26, the starting isochroman (150 mg; .64 mmol) and methanol (25 mg; .76 mmol) were treated with DDQ to afford a crude adduct (160 mg) which was then treated with CAN. This reaction yielded an impure crude quinone (91 mg) which was treated with 1-acetoxy-1,3-butadiene as described in step 4, example 26, affording after chromatographic purification (0-2% ethyl acetate in toluene) the title compound as 18 mg of slightly impure form and 5 mg of pure product (13% overall).

^{1}H NMR ($CDCl_3$, 250 MHz) δ: 1.87 (3H, s, =C-CH_3), 2.49 (1H, dd, J = 11.5 and 19.5Hz, H-4 ax), 2.84 (1H, dd, J = 3.5 and 19.5 Hz, H-4 eq), 3.61 (3H, s, -OCH_3), 4.50 (1H, dd, J = 3.5 and 11.5 Hz, H-3), 5.00 (1H, s, =CH), 5.15 (1H, s, =CH), 5.63 (1H, s, H-1), 7.75 (2H, m, Ar-H), 8.10 (2H, m, Ar-H).

Step 3: **(1'S, 1S, 3R)-5,8-dimethoxy-3-isopropenyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexo-pyranose) isochroman.**

Following the procedure described in the first part of step 3, example 26, the starting isochroman from step 1 herein (250 mg; 1.07 mmol) was treated with α-2,3,6-trideoxy-3-trifluoroacetamido-4-O-p-nitrobenzoyl-L-lyxohexopyranose (461 mg; 1.17 mmol) and DDQ (337 mg; 1.49 mmol) in dichloromethane (20 ml) containing 4Å molecular sieves (500 mg) to yield after chromatography on silica gel using 25% ethyl acetate in hexane with .1% triethylamine, the title compound as a mixture with its (1'S, 1R, 3S) diastereomer (1:1; 310 mg). Another fraction gave pure titled compound (131 mg; 19%).

^{1}H NMR (250 MHz, CD_2Cl_2) δ: 1.22 (3H, d, J = 6.5 Hz, H-6'), 1.83 (3H, s, =C-CH_3), 1.75-2.20 (2H, m, H-2'), 2.48 (1H, dd, J = 12 and 17.5 Hz, H-4 ax), 2.89 (1H, dd, J = 3.5 and 17.5 Hz, H-4 eq), 3.77 (3H, s, OCH_3), 3.78 (3H, s, OCH_3), 4.40-4.65 (2H, m, H-3 and H-3'), 4.73 (1H, q, J = 6.5 Hz, H-5'), 4.92 (1H, s, =CH), 5.09 (1H, s, =CH), 5.42 (1H, br s, H-1'), 5.57 (1H, d, J = 3 Hz, H-4'), 6.12 (1H, s, H-1), 6.31 (1H, br d, J = 6 Hz, N-H), 6.73 and 6.79 (2H, AB doublets, Ar-H), 8.27 (4H, m, PNB).

The (1'S, 1R, 3S)-5,8-dimethoxy-3-isopropenyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexo-pyranose) isochroman had ^{1}H NMR (CD_2Cl_2, 250 MHz) δ: 1.10 (3H, d, J = 6.5 Hz, H-6'), 1.83 (3H, s, =C-CH_3), 1.90-2.20 (2H, m, H-2'), 2.39 (1H, dd, J = 12 and 17.5 Hz, H-4 ax), 2.89 (1H, dd, J = 3.5 and 17.5 Hz, H-4 eq), 3.76 (3H, s, OCH_3), 3.77 (3H, s, OCH_3), 4.35 (1H, q, J = 6.5 Hz, H-5'), 4.50-4.70 (2H, m, H-3 and H-3'), 4.90 (1H, br s, =CH), 5.10 (1H, br s,

=CH), 5.38 (1H, br s, H-1'), 5.54 (1H, br s, H-4'), 5.94 (1H, s, H-1), 6.31 (1H, m, N-H), 6.71 and 6.77 (2H, AB system, Ar-H), 8.27 (4H, m, PNB).

Step 4: (1'S, 1R, 3S)-5,10-dioxo-3-isopropenyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexo-pyranose) 3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran

Using the same procedure as described in step 6 of this example, the starting isochroman from step 3 herein (80 mg; .13 mmol) afforded after CAN oxidation and Diels-Alder the title product (35 mg; 42% overall) contaminated by what looks like aglycone systems.
^{1}H NMR (250 MHz, $CDCl_3$) δ: 1.17 (3H, d, J = 6.5 Hz, H-6'), 1.87 (3H, s, =C-CH_3), 2.09 (2H, m, H-2'), 2.45 (1H, m, H-4 ax), 2.90 (1H, m, H-4 eq), 4.34 (1H, q, J = 6.5 Hz, H-5'), 4.50-4.75 (2H, m, H-3 and H-3'), 5.00 (1H, s, =C-H), 5.17 (1H, s, =C-H), 5.44 (1H, br s, H-1'), 5.72 (1H, s, H-4'), 5.99 (1H, s, H-1), 6.40 (1H, br d, J = 7.5 Hz, NH), 7.75 (2H, m, Ar-H), 8.10 (2H, m, Ar-H), 8.28 (4H, m, PNB).

Step 5: (1'S, 1R, 3S)-5,10-dioxo-3-isopropenyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran (BCH-2153)

Using the procedure described in step 3, example 32, the starting protected alcohol from step 6 herein (slightly impure, 30 mg; .047 mmol) afforded the title compound (11 mg; 48%), M.P.: 170°C (dec).
IR (neat): 3417, 2936, 1716, 1664, 1596, 1293, 1167 and 983 cm^{-1}.
^{1}H NMR (250 MHz, $CDCl_3$) δ: 1.22 (3H, d, J = 6.5 Hz, H-6'), 1.70-2.10 (3H, m, H-2' and O-H), 1.85 (3H, s, =C-CH_3), 2.41 (1H, dd, J = 11.5 and 19.5 Hz, H-4 ax), 2.89 (1H, dd, J = 3.5 and 19.5 Hz, H-4 eq), 3.59 (1H, m, H-4'), 4.16 (1H, q, J = 6.5 Hz, H-5'), 4.35 (1H, m, H-3'), 4.52 (1H, dd, J = 3.5 and 11.5 Hz, H-3), 4.96 (1H, s, =CH), 5.13 (1H, s, =CH), 5.54 (1H, d, J = 3.5 Hz, H-1'), 5.93 (1H, s, H-1), 6.71 (1H, br d, J = 8.5 Hz, -NH), 7.75 (2H, m, Ar-H), 8.10 (2H, m, ArH).

Step 6: (1'S, 1S, 3R)-5,10-dioxo-3-isopropenyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexo-pyranose) 3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran

To a solution of the starting isochroman from step 3 herein (120 mg; 0.19 mmol) in acetonitrile (4 ml) at 0°C was added a solution of CAN (prepared by dissolving ceric ammonium nitrate (630 mg; 1.15 mmol) in water (2 ml) and then adding slowly sodium bicarbonate (169 mg)). After the addition, the mixture was stirred for 10 minutes and was then quenched with saturated sodium bicarbonate solution. The product was extracted with dichloromethane and the combined organic extracts were washed with brine and dried over Na_2SO_4 to yield a crude quinone (112 mg) which was dissolved in toluene (5 ml) and reacted with 1-acetoxy-1,3-butadiene (113 µl; 1 mmol) at room temperature for 15 hours. After this

time, silica gel was added and air was bubbled through for 30 minutes. The residue was applied to a silica gel column and eluted with 0-5% ethyl acetate in toluene affording slightly impure title compound (54 mg) along with pure product (17 mg; total yield 57%).

^{1}H NMR (250 MHz, $CDCl_3$) δ: 1.36 (3H, d, J = 6.5 Hz, H-6'), 1.86 (3H, s, =C-CH_3), 1.99 (1H, br dd, J = 5 and 12.5 Hz, H-2' eq), 2.13 (1H, td, J = 3.5 and 12.5 Hz, H-2' ax), 2.52 (1H, dd, J = 11.5 and 19 Hz, H-4 ax), 2.91 1H, dd, J = 3.5 and 19 Hz, H-4 eq), 4.48 (1H, br d, J = 11.5 Hz, H-3), 4.62 (1H, m, H-3'), 4.84 (1H, q, J = 6.5 Hz, H-5'), 5.00 (1H, br s, =CH), 5.14 (1H, br s, =C-H), 5.47 (1H, br s, H-1'), 5.62 (1H, d, J = 2.5 Hz, H-4'), 6.13 (1H, s, H-1), 6.47 (1H, br d, J = 7.5 Hz, -NH), 7.78 (2H, m, Ar-H), 8.12 (2H, m, Ar-H), 8.29 (4H, m, PNB).

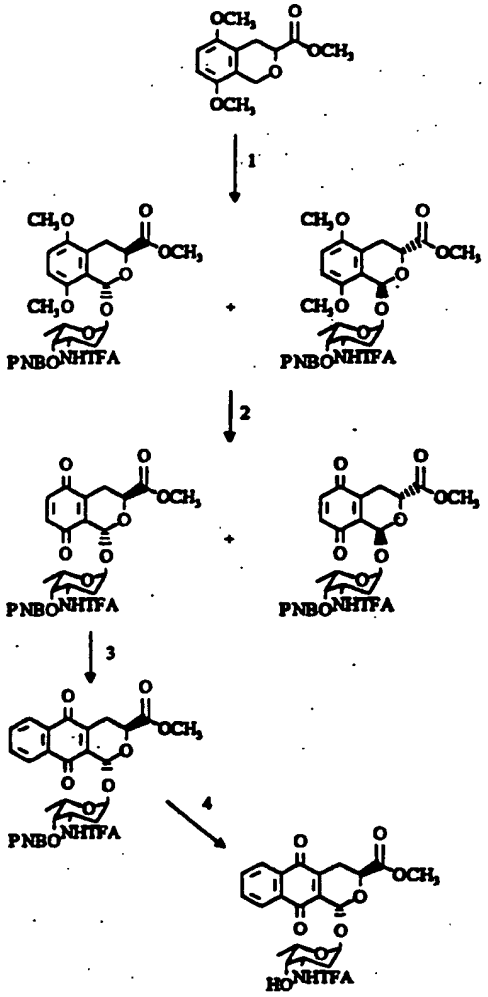
Step 7: **(1'S, 1S, 3R)-5,10-dioxo-3-isopropenyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran (BCH-21-52)**

Using the procedure described in step 3, example 32, the starting protected alcohol from step 6 herein (16 mg; .0248 mmol) afforded the title compound (11 mg; 90%), M.P.: 102-105°C.

IR (neat): 3418, 2934, 1718, 1669, 1295, 1167, 982 and 965 cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$) δ: 1.42 (3H, d, J = 6.5 Hz, H-6'), 1.84 (3H, s, =C-CH_3), 1.86 (2H, m, H-2'), 1.99 (1H, d, J = 8.0 Hz, -OH), 2.51 (1H, dd, J = 11.5 and 19.5 Hz, H-4 ax), 2.89 (1H, dd, J = 3.5 and 19.5 Hz, H-4 eq), 3.65 (1H, m, H-4'), 4.35 (1H, m, H-3'), 4.46 (1H, dd, J = 3.5 and 11.5 Hz, H-3), 4.63 (1H, q, J = 6.5 Hz, H-5'), 4.98 (1H, s, =CH), 5.12 (1H, s =CH), 5.43 (1H, br s, H-1'), 6.07 (1H, s, H-1), 6.72 (1H, m, -NH), 7.75 (2H, m, Ar-H), 8.12 (2H, m, Ar-H).

Example 31: **Preparation of (1'S,1R,3S)-5,10-dioxo-3-methoxycarbonyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran: (BCH-2128)**



BCH-2128

Step 1: **(1'S, 1R, 3S) and (1'S, 1S, 3R)-5,8 dimethoxy-3-methoxycarbonyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-isochroman.**

Using the procedure described in step 2, example 32, the starting isochroman (500 mg; 1.98 mmol) afforded after flash chromatography (5-20% acetone in benzene containing a trace of triethylamine) the mixture of title compounds (490 mg; 40% (~1:1)).

^{1}H NMR (250 MHz, CD_2Cl_2) δ: (for 1'S, 1R, 3S): 1.15 (3H, d, J = 6.5 Hz, H-6'), 1.70-2.25 (2H, m, H-2'), 2.65 (1H, m, H-4 ax), 3.10 (1H, m, H-4 eq), 3.76-3.78 (9H, superimposed singlets, OCH_3), 4.38 (1H, q, J = 6.5 Hz, H-5'), 4.45-4.85 (2H, m, H-3 and H-3'), 5.41 (1H, m, H-1'), 5.57 (1H, m, H-4'), 5.97 (1H, s, H-1), 6.45 (1H, br d, J = 7.5 Hz, -NH), 6.65-6.85 (2H, m, Ar-H), 8.26 (4H, m, PNB); δ (for 1'S, 1S, 3R): 1.22 (3H, d, J = 6.5 Hz, H-6'), 1.70-2.20 (2H, m, H-2'), 2.66 (1H, m, H-4 ax), 3.10 (1H, m, H-4 eq), 3.76-3.78 (9H, superimposed singlets, OCH_3), 4.45-4.85 (3H, m, H-3, H-

3' and H-5'), 5.42 (1H, m, H-1'), 5.57 (1H, m, H-4'), 6.16 (1H, s, H-1), 6.45 (1H, br d, J = 7.5 Hz, -N-H), 6.65-6.85 (2H, m, Ar-H), 8.26 (4H, m, PNB).

Step 2: (1'S, 1R, 3S) and (1'S, 1S, 3R)-5,8 dioxo-3-methoxycarbonyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-5,8-dihydro-isochroman.

To a solution of the starting isochroman from step 1 herein (475 mg; 0.74 mmol) in acetonitrile (15 ml) at 0°C was added a solution of CAN (prepared by dissolving ceric ammonium nitrate (2.42 g) in water (7 ml) and then buffering with sodium bicarbonate (652 mg) added slowly). After the addition, the mixture was stirred at 0°C for 15 minutes and was then quenched with saturated sodium bicarbonate solution and extracted with dichloromethane. The combined organic layers were washed with brine and dried over Na_2SO_4 giving a crude mixture of the title quinones (422 mg; 93%) used as such for the next reaction. ^1H NMR (250 MHz, CD_2Cl_2) δ: 1.15 (3H, d, J = 6.5 Hz, H-6', A*), 1.27 (3H, d, J = 6.5 Hz, H-6', B), 1.70 -2.25 (2H, m, H-2', A and 2H, m, H-2', B), 2.55 (1H, m, H-4 ax, A and 1H, m, H-4 ax, B), 2.85 (1H, m, H-4 eq, A and 1H, m, H-4 eq, B), 3.76 (3H, s, OCH_3, B), 3.77 (3H, s, OCH_3, A), 4.34 (1H, q, J = 6.5 Hz, H-5', A), 4.40-4.70 (2H, m, H-3' and H-3, A and 3H, m, H-3', H-3 and H-5', B), 5.39 (1H, m, H-1', A and 1H, m, H-1', B), 5.54 (1H, d, J =3H, H-4', B), 5.57 (1H, d, J = 3Hz, H-4', A), 5.80 (1H, s, H-1, A), 5.95 (1H, s, H-1, B), 6.60 (1H, m, NH, A and 1H, m, NH, B), 6.80 (2H, m, Ar-H, A and 2H, m, Ar-H, B), 8.26 (4H, m, PNB, A and 4H, m, PNB, B).

* A is (1'S, 1R, 3S) diastereomer and B is (1'S, 1S, 3R) diastereomer.

Step 3: (1'S, 1R, 3S)-5,10-dioxo-3-methoxycarbonyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran.

Using the procedure described in step 4, example 26, the starting quinone from step 2 herein (400 mg; .658 mmol of a 1:1 mix of 1'S, 1R, 3S and 1'S, 1S, 3R) afforded pure title product (13 mg) along with a ~1:1 mixture of (1'S, 1R, 3S) and (1'S, 1S, 3R) isomers (275 mg).

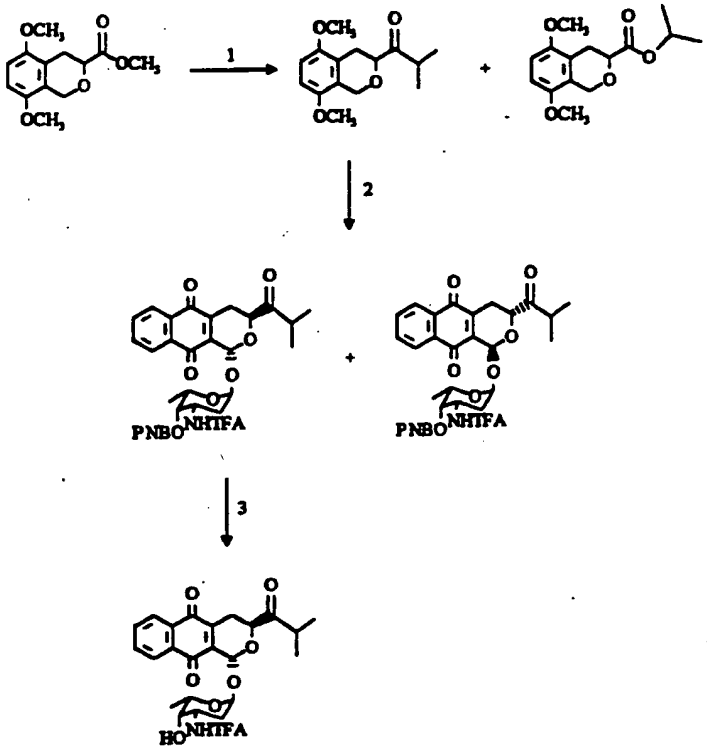
^1H NMR (250 MHz, CD_2Cl_2) δ: 1.18 (3H, d, J = 6.5 Hz, H-6'), 1.90-2.20 (2H, m, H-2'), 2.68 (1H, dd, J = 11.5 and 19 Hz, H-4 ax), 3.08 (1H, dd, J = 4 and 19 Hz, H-4 eq), 3.80 (3H, s, OCH_3), 4.38 (1H, q, J = 6.5 Hz, H-5'), 4.57 (1H, m, H-3'), 4.75 (1H, dd, J = 4 and 11.5 Hz, H-3), 5.42 (1H, br s, H-1'), 5.69 (1H, br s, H-4'), 5.99 (1H, s, H-1), 6.42 (1H, br d, J = 7 Hz, -NH), 7.75 (2H, m, Ar-H), 8.08 (2H, m, Ar-H), 8.28 (4H, m, PNB).

Step 4: (1'S, 1R, 3S)-5,10-dioxo-3-methoxycarbonyl-1-(2',3',6',trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyrano (BCH-2128)

Using the procedure described in step 5, example 26, the starting protected alcohol from step 3 herein (12 mg; 0.018 mmol) afforded after column chromatography (10% acetone in dichloromethane), the title compound (5 mg; 54%) as a yellow solid. M.P. 92-105°C.

^{1}H NMR (250 MHz, CD_2Cl_2) δ: 1.22 (3H, d, J = 6.5 Hz, H-6'), 1.55 (1H, br s, OH), 1.70-2.00 (2H, m, H-2'), 2.66 (1H, dd, J = 12.0 and 19.0 Hz, H-4 ax), 3.06 (1H, dd, J = 4.0 and 19.0 Hz, H-4 eq), 3.59 (1H, br s, H-4'), 3.79 (3H, s, $-CO_2CH_3$), 4.17 (1H, q, J = 6.5 Hz, H-5'), 4.28 (1H, m, H-3'), 4.73 (1H, dd, J = 4.0 and 11.5 Hz, H-3), 5.52 (1H, br s, H-1'), 5.92 (1H, s, H-1), 6.75 (1H, m, -NH), 7.75 (2H, m, Ar-H), 8.05 (2H, m, Ar-H).

Example 32: **Preparation of (1'S,1R,3S)-isopropyl-[5,10-dioxo-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyranyl]-ketone: (BCH-2112)**



BCH-2112

Step 1: **isopropyl-(5,8-dimethoxy-isochroman-3-yl)-ketone**

To a solution of the starting ester (1.0 g; 3.97 mmol) in tetrahydrofuran (30 ml) at 0°C was added isopropyl magnesium chloride (2M, 4.17 mmol). The mixture was stirred at 0°C for 20 minutes and at room temperature for 1 hour. It was then quenched with saturated ammonium chloride solution and extracted with dichloromethane. The combined organic layers were washed with brine and dried over $MgSO_4$ to afford after evaporation, the title compound (240 mg; 23% (40% based on S.M. recovered)). ^1H NMR (250 MHz, $CDCl_3$) δ: 1.13 (3H, d, J = 6.5 Hz, $C\underline{H}_3$-CH), 1.16 (3H, d, J = 6.5 Hz, $C\underline{H}_3$-CH), 2.59 (1H, br dd, J = 11.5 and 17 Hz, H-4 ax), 3.04 (1H, dm, J = 17 Hz, H-4 eq), 3.17 (1H, m, $C\underline{H}$-CH_3), 3.76 (3H, s, OCH_3), 3.78 (6H, s, OCH_3), 4.17 (1H, dd, J = 3.5 and 11.5 Hz, H-3), 4.64 (1H, br d, J = 16 Hz, H-1), 5.03 (1H, d, J = 16 Hz, H-1), 6.65 (2H, AB system, Ar-H).

5,8-dimethoxy-3-isopropoxycarbonyl-isochroman was obtained as a by-product resulting from oxidation of the Grignard reagent.

^1H NMR (250 MHz, $CDCl_3$) δ: 1.29 (3H, d, J = 6Hz, $C\underline{H}_3$-CH), 1.30 (3H, d, J = 6 Hz, $C\underline{H}_3$-CH), 2.74 (1H, br dd, J = 11 and 17 Hz, H-4 ax), 3.05 (1H, dm, J = 17 Hz, H-4 eq), 3.75 (3H, s, OCH_3),

3.78 (3H, s, OCH_3), 4.19 (1H, dd, J = 4 and 11 Hz, H-3), 4.65 (1H, br d, J = 16 Hz, H-1), 5.04 (1H, d, J = 16 Hz, H-1), 5.15 (1H, sept., J = 6 Hz, C<u>H</u>-CH_3), 6.64 (2H, AB system, Ar-H).

Step 2: **(1'S, 1R, 3S)-isopropyl-[1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyranyl]-ketone**

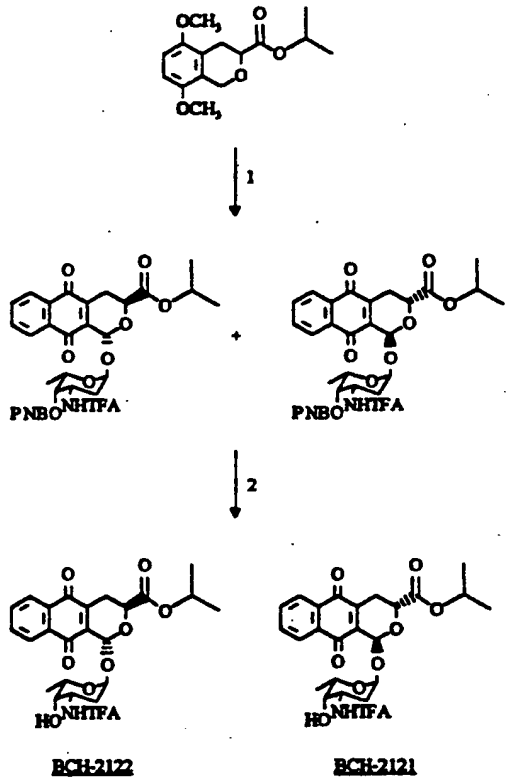
To a solution of α-2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose (408 mg; 1.04 mmol) and starting ketone from step 1 herein (230 mg; 0.87 mmol) in dichloromethane (15 ml), were added 4Å molecular sieves (400 mg) and 2,3-dichloro-5,6-dicyano-benzoquinone (270 mg; 1.2 mmol). The mixture was stirred at room temperature for 14 hours and was then quenched with saturated bicarbonate solution and extracted with dichloromethane. The combined organic layers were washed with brine and dried over Na_2SO_4 to afford a crude adduct (590 mg) which was dissolved in acetonitrile (20 ml) at 0°C and treated dropwise with a solution of ceric ammonium nitrate (3.15 g; 5.7 mmol) in water (10 ml) containing sodium bicarbonate (847 mg). After the addition, the mixture was stirred at 0°C for 15 minutes and was quenched with saturated $NaHCO_3$ and extracted with dichloromethane. The combined organic layers were washed with brine and dried over Na_2SO_4 to afford a crude quinone mixture (557 mg) of which 100 mg (.16 mmol) were dissolved in toluene (6 ml) and treated with 1-acetoxy-1,3-butadiene (113 µl; 1 mmol) at room temperature for 14 hours. Silica gel was added to the mixture and air was bubbled through for 1 hour while toluene partly evaporated. The residue was applied to a column of silica gel and eluted with 0-10% ethyl acetate in toluene affording the title compound (20 mg) slightly contaminated by its (1S, 3R) diastereomer (~3:1).
^1H NMR (250 MHz, $CDCl_3$) δ: 1.00-1.30 (9H, m, H-6' and CH-($C\underline{H}_3$)$_2$), 1.60-2.40 (2H, m, H-2'), 2.52 (1H, m, H-4 ax), 3.00-3.35 (2H, m, H-4 eq and C<u>H</u>-(CH_3)$_2$), 4.32 (1H, q, J = 6.5 Hz, H-5'), 4.50-4.90 (2H, m, H-3 and H-3'), 5.44 (1H, br s, H-1'), 5.75 (1H, br s, H-4'), 6.06 (1H, s, H-1), 6.49 (1H, br d, J = 7.5 Hz, -NH), 7.78 (2H, m, Ar-H), 8.07 (2H, m, Ar-H), 8.27 (4H, m, PNB), apparent signals for (1S, 3R) diastereomer are: 6.22 (1H, s, H-1) and 6.58 (1H, br d, J = 7.5 Hz, NH).

Step 3: **(1'S, 1R, 3S)-isopropyl-[1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyranyl]-ketone (BCH-2112)**

To a solution of starting protected alcohol from step 2 herein (20 mg; 0.0296 mmol) in methanol (.3 ml): tetrahydrofuran (1 ml) at 0°C was added sodium methoxide in methanol (4.37 M; .7 µl; .1 eq). The mixture was stirred at 0°C for 20 minutes and was then quenched with saturated NH_4Cl solution and was extracted with dichloromethane. The combined organic layers were washed with brine and dried over Na_2SO_4 to afford a crude residue which was purified by column chromatography on silica gel using 10% acetone in benzene yielding the titled compound (6.4 mg; 63%).

^1H NMR (CD_2Cl_2, 250 MHz), δ: 1.11 (6H, d, J = 6.5 Hz, -CH-(CH_3)$_2$), 1.20 (3H, d, J = 6.5 Hz, H-6'), 1.65 (1H, s, OH), 1.75-2.05 (2H, m, H-2'), 2.48 (1H, dd, J = 11.5 and 19.5 Hz, H-4 ax), 3.01 (1H, dd, J = 4.0 and 19.5 Hz, H-4 eq), 3.15 (1H, sept., J = 6.5 Hz, C<u>H</u>-(CH_3)$_2$), 3.58 (1H, d, J = 2.5 Hz, H-4'), 4.10 (1H, q, J = 7.0 Hz, H-5'), 4.28 (1H, m, H-3'), 4.68 (1H, dd, J = 4.0 and 11.5 Hz, H-3), 5.55 (1H, d, J = 3.5 Hz, H-1'), 5.97 (1H, s, H-1), 6.72 (1H, m, N-H), 7.75 (2H, m, Ar-H), 8.05 (2H, m, Ar-H).

Example 33: **Preparation of (1'S,1S,3R) and (1'S,1R,3S)-5,10-dioxo-3-isopropoxycarbonyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran: (BCH-2122) and (BCH-2121)**



BCH-2122 BCH-2121

Step 1: **(1'S, 1R, 3S), and (1'S, 1S, 3R)-5,10-dioxo-3-isopropoxycarbonyl-1-(2',3',6'-trideoxy-3',trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran**

Using the procedure described in step 2, example 32, the starting isochroman from step 1, example 32, (300 mg; 1.07 mmol) afforded a crude glycosylated adduct (417 mg) which was treated with CAN to give a crude quinone mixture (355 mg) of which 250 mg were reacted with acetoxybutadiene. This reaction

yielded a slightly impure mixture of the title compounds (113 mg; 15% overall) (~55:45) favoring the (1'S, 1R, 3S) isomer.

^{1}H NMR (250 MHz, $CDCl_3$) δ: (for 1'S, 1R, 3S): 1.15-1.42 (9H, m, H-6' and CH-(CH_3)$_2$), 1.90-2.20 (2H, m, H-2'), 2.68 (1H, dd, J = 12 and 19 Hz, H-4 ax), 3.12 (1H, m, H-4 eq), 4.40 (1H, q, J = 6.5 Hz, H-5'), 4.50-4.80 (2H, m, H-3 and H-3'), 5.18 (1H, m, C$\underline{H}$-(CH_3)$_2$), 5.44 (1H, br s, H-1'), 5.74 (1H, br s, H-4'), 6.03 (1H, s, H-1), 6.55 (1H, br d, J = 7.5 Hz, N-H), 7.77 (2H, m, Ar-H), 8.11 (2H, m, ArH), 8.27 (4H, m, PNB); (for 1'S, 1S, 3R): 1,15-1.42 (9H, m, H-6' and CH($C\underline{H}_3$)$_2$), 1.90-2.20 (2H, m, H-2'), 2.69 (1H, dd, J = 12 and 19 Hz, H-4 ax), 3.12 (1H, m, H-4 eq), 4.50-4.80 (3H, m, H-3, H-3' and H-5'), 5.18 (1H, m, C$\underline{H}$(CH_3)$_2$), 5.45 (1H, br s, H-1'), 5.65 (1H, d, J = 3 Hz, H-3'), 6.18 (1H, s, H-1), 6.61 (1H, br d, J = 7.5 Hz, -NH), 7.77 (2H, m, Ar-H), 8.11 (2H, m, Ar-H), 8.27 (4H, m, PNB).

Step 2: **(1'S, 1R, 3S)-5,10-dioxo-3-isopropoxycarbonyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran (BCH-2122)**

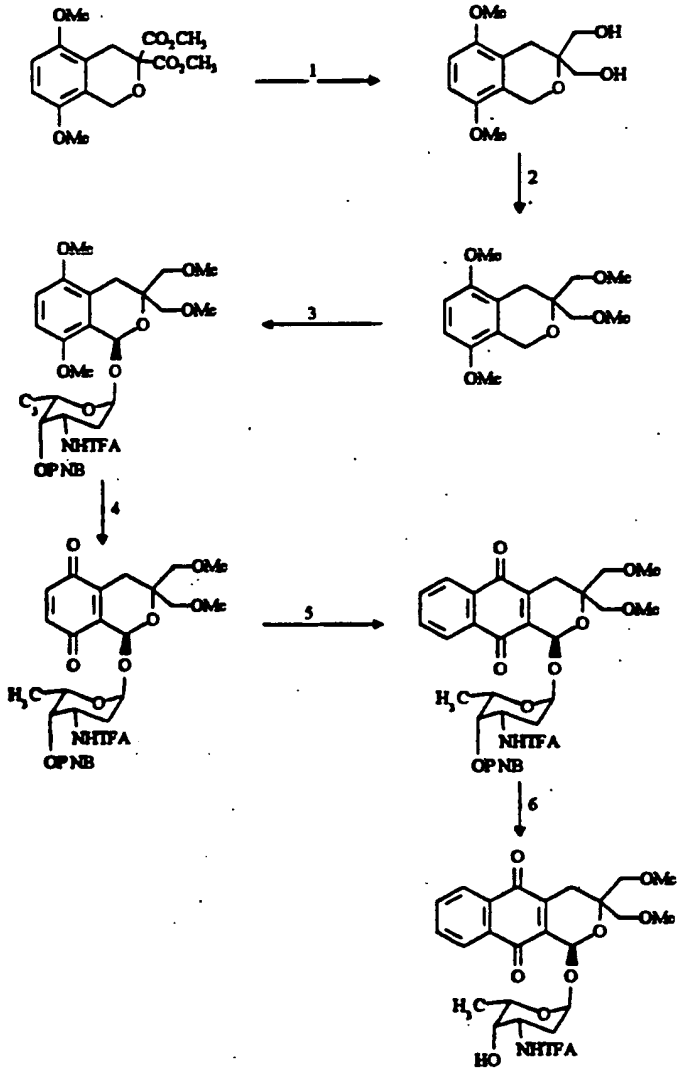
Using the procedure described in step 3, example 32, the starting protected alcohol from step 1 herein (113 mg; .16 mmol) afforded (after multiple chromatographic separations using 10% acetone in benzene or in dichloromethane) the pure title compound (7 mg; 8%). M.P.: 93-101°C.

^{1}H NMR ($CDCl_3$) δ: 1.29 and 1.33 (6H, 2d, J = 6.5 Hz, -CH-($C\underline{H}_3$)$_2$), 1.33 (3H, d, J = 6.5 Hz, H-6'), 1.70-2.10 (3H, m, H-2' and O-H), 2.68 (1H, dd, J = 11.5 and 19.5 Hz, H-4 ax), 3.11 (1H, dd, J = 4.0 and 19.5 Hz, H-4 eq), 3.65 (1H, m, H-4'), 4.21 (1H, q, J = 6.5 Hz, H-5'), 4.38 (1H, m, H-3'), 4.66 (1H, dd, J = 4.0 and 11.5 Hz, H-3), 5.18 (1H, sept., J = 6.5 Hz, C$\underline{H}$-(CH_3)$_2$), 5.56 (1H, br s, H-1'), 5.98 (1H, s, H-1), 6.72 (1H, m, N$\underline{H}$), 7.75 (2H, m, Ar-H), 8.10 (2H, m, Ar-H).

(1'S, 1S, 3R)-5,10-dioxo-3-isopropoxycarbonyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L,-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran (BCH-2121) was isolated after multiple chromatographic separations (5 mg; 6%). M.P.: 155°C (dec).

^{1}H NMR ($CDCl_3$) δ: 1.32 (6H, d, J = 6.5 Hz, CH-($C\underline{H}_3$)$_2$), 1.41 (3H, d, J = 6.5 Hz, H-6'), 1.87 (2H, m, H-2'), 2.05 (1H, m, OH), 2.70 (1H, dd, J = 12.0 and 19.5 Hz, H-4 ax), 3.10 (1H, dd, J = 4.0 and 19.5 Hz, H-4 eq), 3.63 (1H, m, H-4'), 4.32 (1H, m, H-3'), 4.55 (1H, q, J = 6.5 Hz, H-5'), 4.62 (1H, dd, J = 4.0 and 12.0 Hz, H-3), 5.16 (1H, sept., J = 6.5 Hz, C$\underline{H}$-(CH_3)$_2$), 5.47 (1H, br s, H-1'), 6.14 (1H, s, H-1), 6.75 (1H, m, N-H), 7.75 (2H, m, Ar-H), 8.12 (2H, m, Ar-H).

Example 34: **Preparation of (1'S,1S)-5,10-dioxo-3,3-dimethoxymethyl-1-(2',3'6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-isochroman (BCH-1697)**



Step 1: **5,8-dimethoxy-3,3 bis (dihydroxymethyl)-isochroman**

Under argon atmosphere, 110 mg (2.90 mmol) of LAH were added to 15 ml of dry THF, previously cooled to 0°C. To this solution was added 0.450 g (1.45 mmol) of 5,8-dimethoxy-3,3-bis (dicarbomethoxy)-isochroman dissolved in 15 ml of THF. The temperature was allowed to warm up to room temperature, and stirring was continued for 3 hours. After that time, another 160 mg (4.22 mmol) of LAH was then added and the reaction mixture was stirred for another hour. After that time, the reaction mixture was poured into 50 ml of a 0.1 N aqueous solution of HCl. Extractions of the aqueous

layer are done using CH_2Cl_2. The combined organic layers are dried over Na_2SO_4, filtered, and the solvent is removed. The isolated titled compound is used without further purification (0.333 g; 90%).
NMR ^1H (250 MHz) ($CDCl_3$:ppm): 6.64 (2H, 2d, aromatics); 4.80 (2H, s, H_{1a}- H_{1b}); 3.76 (6H, s, 2xOCH_3); 3.71 (4H, m, 2-CH_2-); 2.53 (2H, s, 2xOH); 1.85 (2H, m, H_{4a}-H_{4b}).

Step 2: 5,8-dimethoxy-3,3 bis (dimethoxymethyl)-isochroman

Under argon atmosphere, 0.333 g (1.31 mmol) of the starting material from step 1 herein were placed in 70 ml of dry THF. To this solution were then added 0.105 g (2.62 mmol) of NaH. After a few minutes of stirring, 0.41 ml (6.55 mmol) of MeI were added to the reaction mixture and stirring was left for 1.5 hour. After that time, another 0.145 g of NaH and 0.7 ml of MeI were added to the reaction which was completed after another hour of stirring. Aqueous HCl (0.1 N) was then added and extractions were done using CH_2Cl_2. The combined organic extracts were washed with an aqueous solution of sodium bicarbonate, dried over Na_2SO_4, filtered, and the solvent was removed. The obtained titled compound was used for next step without further purification. Isolated product (0.470 g; >99%).
NMR ^1H (250 MHz) ($CDCl_3$:ppm): 7.26 (2H, 2d, aromatics); 4.74 (2H, s, H_{1a}-H_{1b}); 3.76 (6H, 2s, 2xOCH_3); 3.54 (2H, d, J = 9.7 Hz, -CH_2- side chain); 3.41 (2H, d, J = 9.7 Hz, -CH_2- side chain); 3.38 (6H, s, 2xOCH_3); 2.64 (2H, s, H_{4a}-H_{4b}).
IR (film) (cm^{-1}) 2925 (CH aliphatic), 1580 (C=C), 1475 (CH_2), 1450 and 1360 (CH_3), 1100 and 1248 (C-O).

Step 3: (1'S, 1S)-5,8-dimethoxy-3,3-dimethoxymethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-isochroman

Under argon atmosphere, the following reagents: product from step 2 herein, 0.477 g (1.70 mmol), 2,3,6-trideoxy-3-trifluoroacetamido-4-O-p-nitrobenzoyl-α-L-lyxohexopyranose 0.378 g (2.00 mmol) and DDQ 0.452 g (2.00 mmol) were dissolved in 50 ml of dichloromethane. The reaction mixture was stirred at room temperature for a period of 16 hours. After that time, an excess of DDQ was then added to the reaction mixture and stirring was left for another hour. The reaction mixture was then quenched with aquous NH_4Cl and extractions of the aqueous layer was done using CH_2Cl_2. The combined organic layers were dried over Na_2SO_4, filtered and the solvent was removed. The crude material was purified by flash chromatography; eluent:hexanes-ethyl acetate (70:30) then (60:40). The obtained titled compound was a pale yellow solid (0.434 g; 39%).
NMR ^1H (250 MHz) (C_6D_6; ppm): 7.89 (2H, m, aromatics), 7.68 (2H, m, aromatics), 6.53 (2H, m, aromatics), 6.52 (1H, NH), 6.08 (1H, s, H_1), 5.62 (1H, s, $H_{1'}$), 4.70 (1H, m, $H_{5'}$), 4.60 (1H, m, $H_{3'}$), 3.82 (2H, m, CH_2-OMe), 3.74 (1H, m, $H_{4'}$), 3.55 (2H, m, CH_2-OMe), 3.48 and 3.42 (6H, 2s, 2xOCH_3), 3.40 (2H, m, $H_{2'a}$ and $H_{2'b}$), 3.18 and 3.11 (6H, 2s, 2xOCH_3), 2.13 (1H, m, H_{4a}), 1.86 (1H, m, H_{4b}), 1.21 (3H, d, J = 6.2 Hz, CH_3 sugar).

Step 4: (1'S, 1S)-5,8-dioxo-3,3-dimethoxymethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-isochroman

The starting material from step 3 herein, 0.430 g (0.65 mmol), was dissolved in acetonitrile at 0°C. A solution of $NaHCO_3$ 0.107 g (1.30 mmol) in 7 ml of water was then added and the solution was stirred for 10 minutes. After that time, 1.053 g (1.95 mmol) of CAN diluted in 12 ml of water were then added to the reaction mixture in a dropwise manner. The reaction was complete after 10 minutes. A very diluted solution of $NaHCO_3$ in water was then added to the reaction mixture. Extractions of the reaction mixture were done using CH_2Cl_2. The combined organic layers are dried over Na_2SO_4, filtered and the solvent was removed. The titled compound was used for next step without further purification, (0.387 g; 95%).

NMR ^1H (250 MHz) (C_6D_6; ppm): 7.94 (2H, d, J = 7.5 Hz, aromatics), 7.75 (2H, d, J = 7.5 Hz, aromatics), 7.42 (1H, m, NH), 6.20 (2H, m, quinone ring), 5.98 (1H, s, H_1), 5.92 (1H, s, $H_{1'}$), 5.41 (1H, s, $H_{4'}$), 4.90 (1H, q, $H_{5'}$), 4.67 (1H, m, $H_{3'}$), 3.47 (2H, CH_2-OMe), 3.29 (2H, CH_2-OMe), 3.16 (3H, s, OCH_3), 3.11 (3H, s, OCH_3), 2.50 (2H, 2d, $H_{2'a}$, $H_{2'b}$), 2.22 (1H, m, H_{4a}), 1.97 (1H, m, H_{4b}), 1.27 (3H, d, J = 6.3 Hz, -CH_3 sugar).

Step 5: (1'S, 1S)-5,10-dioxo-3,3-dimethoxymethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c] pyran

Under argon atmosphere, 0.173 g (0.27 mmol) of the product from step 4 herein was dissolved in 10 ml of dry toluene. To this solution was added 0.2 ml (1.65 mmol) of 1-acetoxy-1,3-butadiene. The reaction mixture was left stirring overnight at room temperature. Silica gel was then added to the reaction mixture and air was bubbled in it for a period of 2 hours. Whitout removing the solvent, the reaction mixture was put on top of a silica gel column and toluene was used as the first eluent. Toluene-ethyl acetate (1:1) was then used to elute the desired compound. The titled compound was isolated (0.06 g, 32%) as a yellow solid.

NMR ^1H (250 MHz) (CD_2Cl_2; ppm): 8.29 (4H, m, aromatics), 8.07 (2H, m, aromatics), 7.76 (2H, m, aromatics), 6.45 (1H, d, NH), 6.05 (1H, s, H_1), 5.70 (1H, s, $H_{1'}$), 5.43 (1H, s, $H_{3'}$), 4.82 (1H, m, $H_{5'}$), 4.52 (1H, m, $H_{4'}$), 3.27-3.52 (4H, m, 2x-CH_2- side chains), 3.35 (3H, s, OCH_3), 3.27 (3H, s, OCH_3), 2.72 (2H, 2d overlapped, H_{4a} and H_{4b}), 1.87-2.18 (2H, m, -CH_2- sugar), 1.28 (3H, d, J = 6.5 Hz, -CH_3 sugar).

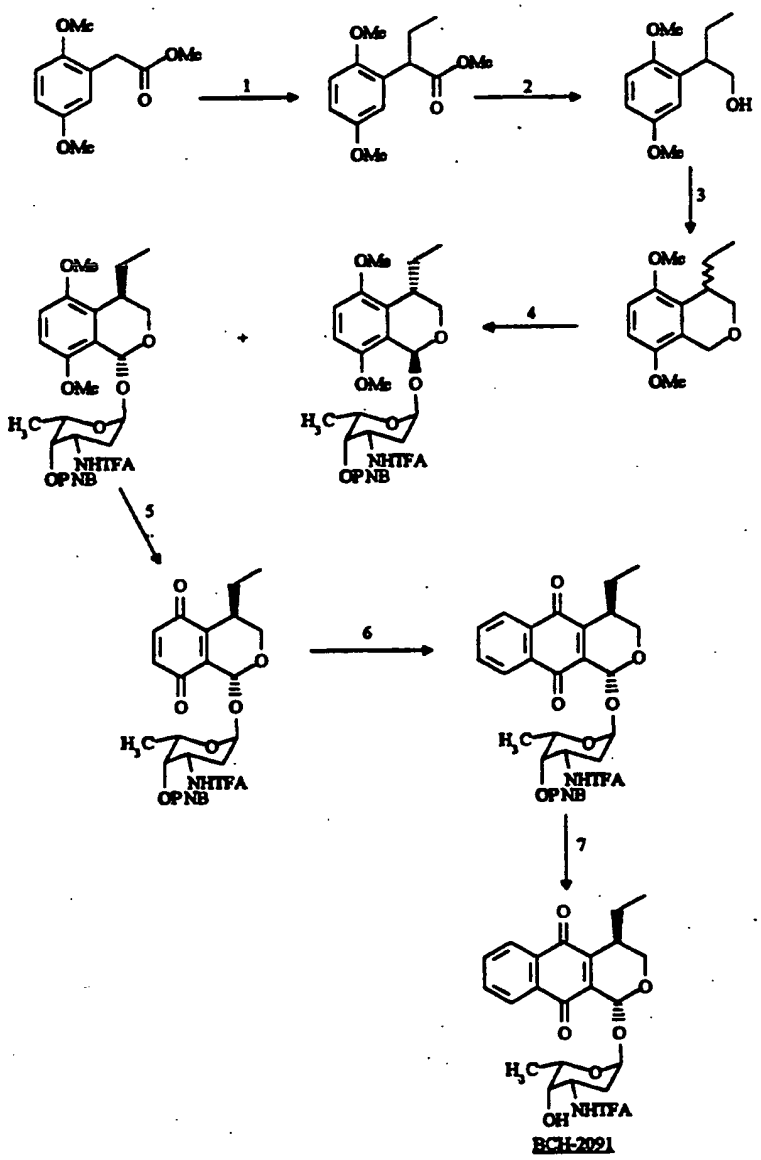
Step 6: (1'S, 1S)-5,10-dioxo-3,3-dimethoxymethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexo-pyranose)-isochroman (BCH-1697)

Under argon atmosphere, the product from step 5 herein, 0.06 g (0.09 mmol) was dissolved in a mixture of 5 ml of dry methanol and 2 ml of dry THF. This solution was cooled to 0°C. 2 µl of a 4.37 M solution of sodium methoxide in methanol were then added to the reaction mixture. The reaction was completed in 10 minutes, it was then quenched by adding aqueous NH_4Cl. Extractions of the aqueous layer was done using dichloromethane. The combined organic layers were dried over Na_2SO_4, filtered and the solvent was removed. The crude material was then purified by flash chromatography, eluent:ethyl acetate-dichloromethane (35:75). The isolated titled compound was a yellow solid (0.03 g, 67%).

NMR ^1H (250 MHz) ($CDCl_3$; ppm): 8.05 (2H, m, aromatics), 7.74 (2H, m, aromatics), 6.81 (1H, d, NH), 6.00 (1H, s, H_1), 5.49 (1H, d, J = 2.8 Hz, $H_{1'}$), 4.58 (1H, q, $H_{5'}$), 4.23 (1H, m, $H_{4'}$), 3.60 (1H, d, J = 2.3 Hz, $H_{3'}$), 3.45 (2H, m, $-CH_2$-(OMe)), 3.37 (2H, m, $-CH_2$-(OMe)), 3.34 (3H, s, OCH_3), 3.25 (3H, s, OCH_3), 2.71 (2H, d, J = 3.5 Hz, H_{4a} and H_{4b}), 2.09 (1H, $_{(broad)}$s, OH), 1.79 (2H, m, $-CH_2$- sugar), 1.32 (3H, d, J = 6.6 Hz, $-CH_3$ sugar).

IR (film) (cm^{-1}): 3450 (OH bonded), 2950 (CH aliphatic), 1675 (C=C), 1000 and 1290 (C-O).

Example 35: **Preparation of (1'S,1R,4R)-5,10-dioxo-4-ethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c] pyran (BCH-2091)**



Step 1: **methyl-2-(2',5'-dimethoxyphenyl) butanoate**

Under argon atmosphere, 3.08 ml (26.16 mmol) of diisopropylamine was added to 85 ml of THF precooled to 0°C. n-BuLi 10.5 ml (26.16 mmol) was then added to this solution and this mixture was then stirred for 30 minutes. After that time, the reaction mixture was cooled to -78°C and the ester 5.00 g (23.78 mmol), 208-186-01 in 65 ml of THF was then added dropwise. After the addition, the mixture was stirred for 5 minutes before HMPA 4.55 ml (26.16 mmol) was added. After another 10 minutes of stirring following the last addition, ethyliodide 5.0 ml (47.56 mmol) was then added to the reaction

mixture. The reaction mixture was then stirred for 30 minutes before removal of the dry ice-acetone bath to allow the temperature to reach room temperature and the reaction was monitored by TLC. The reaction mixture was left stirring at room temperature for 15 hours. The reaction mixture was then quenched by adding aqueous NH_4Cl and extracting with ether. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and the solvent was removed. The crude was purified by flash chromatography using hexanes-ethyl acetate as eluent; 3.36 g of pure titled compound as a white solid were obtained.

NMR ^1H (250 MHz) ($CDCl_3$; ppm): 6.84 (1H, m, aromatic), 6.76 (2H, m, aromatics), 3.90 (1H, t, J = 7.6 Hz, H_3), 3.77 (3H, s, OCH_3), 3.75 (3H, s, OCH_3), 3.64 (3H, s, (CO_2)-CH_3), 2.03 (1H, m, H_{3a}), 1.72 (1H, m, H_{3b}), 0.88 (3H, t, J = 7.3 Hz, -CH_3 terminal).

Step 2: 2-(2',5'-dimethoxyphenyl)-1-butanol

Under argon atmosphere, the product from step 1 herein, 3.36 g (14.08 mmol) was dissolved in 100 ml of dichloromethane. This solution was cooled to 0°C and DIBAL-H, 31.0 ml (30.98 mmol) was added in a dropwise manner. The reaction was complete after 20 minutes so HCl 1N was then added to the reaction mixture and extractions were done using dichloromethane. The combined organic layers were dried over Na_2SO_4, filtered, and the solvent was removed. The isolated titled compound was used for next step without further purification.

NMR ^1H (250 MHz) ($CDCl_3$; ppm): 6.76 (3H, m, aromatics), 3.77 (3H, s, OCH_3), 3.76 (3H, s, OCH_3), 3.75 (2H, m, H_{1a} and H_{1b}), 3.19 (1H, m, H_2), 1.74 (2H, m, H_{3a} and H_{3b}), 1.51 (1H, t, J = 6.2 Hz, OH), 0.85 (3H, t, J = 7.4 Hz, -CH_3 terminal).

Step 3: 5,8-dimethoxy-4-ethyl-isochroman

Under argon atmosphere, the product from step 2 herein, 2.74 g (13.03 mmol) was dissolved in 55 ml of dry ether. Dimethoxy methane 1.65 ml (19.55 mmol) and boron trifluoro etherate 4.9 ml (39.09 mmol) were then added to this solution. The obtained reaction mixture was left stirring overnight. The reaction mixture was quenched using aqueous $NaHCO_3$ and extractions were done using ether. The combined organic extracts were dried over Na_2SO_4, filtered, and the solvent was removed. The residue was purified by flash chromatography using hexanes-ethyl acetate (80:20) and (70:30) as eluent. The isolated titled product was a white solid (1.56 g; 54%).

NMR ^1H (250 MHz) ($CDCl_3$; ppm): 6.64 (2H, m, aromatics), 4.85 (1H, d, J = 16.1 Hz, H_{1a}), 4.55 (1H, d, J = 16.0 Hz, H_{1b}), 4.09 (1H, d, J = 11.3 Hz, H_{3a}), 3.79 (3H, s, OCH_3), 3.75 (3H, s, OCH_3), 3.58 (1H, dd, J_1 = 2.7 Hz, J_2 = 11.4 Hz, H_{3b}), 2.62 (1H, m, H_4), 1.67 (2H, m, -CH_2-ethyl), 1.01 (3H, t, J = 7.5 Hz, -CH_3).

Step 4: (1'S, 1R, 4R)-5,8-dimethoxy-4-ethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexo-pyranose)-isochroman

The titled compound was obtained by applying the procedure from step 3, example 34, to the isochroman from step 3 herein.

NMR ^1H (250 MHz) (C_6D_6; ppm): 7.81 (2H, d, J = 8.8 Hz, aromatics), 7.65 (2H, d, J = 8.9 Hz, aromatics), 6.48 (2H, dd, J_1 = 9.0 Hz, J_2 = 18.1 Hz, aromatics), 6.35 (1H, s, H_1), 6.26 (1H, d, J = 6.9 Hz, NH), 5.81 (1H, s, $H_{1'}$), 5.52 (1H, s, $H_{3'}$), 4.75 (1H, q, $H_{5'}$), 4.58 (1H, m, $H_{4'}$), 4.24 (1H, dd, J_1 = 2.9 Hz, J_2 = 11.4 Hz, H_{3a}), 3.88 (1H, d, J = 11,.4 Hz, H_{3b}), 3.38 (3H, s, OCH_3), 3.37 (3H, s, OCH_3), 2.84 (1H, m, H_4), 1.89 (2H, m, -CH_2- sugar), 1.85-1.55 (2H, m, -CH_2- side chain), 1.18 (3H, d, J = 6.6 Hz, -CH_3 sugar), 1.05 (3H, t, J = 7.3 Hz, -CH_3 side chain).

(1'S, 1S, 4S)-5,8-dimethoxy-4-ethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexo-pyranose)-isochroman was also obtained.

NMR ^1H (250 MHz) (C_6D_6; ppm): 7.81 (2H, d, J = 8.7 Hz, aromatics), 7.61 (2H, d, J = 8.7 Hz, aromatics), 6.54 (2H, m, aromatics), 6.55 (1H, NH), 6.09 (1H, s, H_1), 5.69 (1H, s, $H_{1'}$), 5.45 (1H, s, $H_{3'}$), 4.72 (1H, m, $H_{4'}$), 4.32 (1H, m, $H_{5'}$), 4.26 (1H, dd, J_1 = 2.9 Hz, J_2 = 11.4 Hz, H_{3a}), 3.89 (1H, d, J = 11.2 Hz, H_{3b}), 3.45 (3H, s, OCH_3), 3.39 (3H, s, OCH_3), 2.80 (1H, m, H_4), 1.88 (2H, m, -CH_2- sugar), 1.82 (2H, m, -CH_2- side chain), 1.12 (3H, d, J = 6.4 Hz, CH_3 sugar), 1.04 (3H, t, J = 7.4 Hz, -CH_3 side chain).

Step 5: **(1'S, 1R, 4R)-5,8-dioxo-4-ethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-isochroman**

The (1'S,1R,4R) glycoside from step 4 herein was oxidatively demethylated as per procedure described in step 4, example 34. The titled compound had:

NMR ^1H (250 MHz) (C_6D_6; ppm): 7.80 (2H, d, J = 8.9 Hz, aromatics), 7.62 (2H, d, J = 8.8 Hz, aromatics), 6.89 (1H, d, J = 6.9 Hz, NH), 6.04 (2H, dd, J_1 = 10.1 Hz, J_2 = 18.3 Hz, quinone ring), 5.87 (1H, s, H_1), 5.63 (1H, s, $H_{1'}$), 5.16 (1H, s, $H_{3'}$), 4.80 (1H, q, J = 6.5 Hz, $H_{5'}$), 4.56 (1H, m $H_{4'}$), 3.75 (1H, dd, J_1 = 3.0 Hz, J_2 = 11.6 Hz, H_{3a}), 3.54 (1H, d, J = 11.5 Hz, H_{3b}), 2.25 (1H, m, H_4), 1.89 (2H, m, -CH_2- sugar), 1.47 (2H, m, -CH_2- side chain), 1.27 (3H, d, J = 6.5 Hz, -CH_3 sugar), 0.86 (3H, t, J = 7.3 Hz, -CH_3 side chain).

Step 6: **(1'S, 1R, 4R)-5,10-dioxo-4-ethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran**

The titled compound was obtained in 19% yield following cycloaddition between the quinone from step 5 herein and 1-acetoxybutadiene, as per procedure as described in step 5, example 34.

NMR ^1H (250 MHz) (C_6D_6; ppm): 8.02 (2H, m, aromatics), 7.77 (2H, d, J = 8.9 Hz, aromatics), 7.63 (2H, d, J = 8.9 Hz, aromatics), 6.02 (2H, m, aromatics), 6.53 (1H, d, NH), 6.11 (1H, s, H_1), 5.67 (1H, d, $H_{1'}$), 4.97 (1H, s, $H_{3'}$), 4.95 (1H, m, $H_{4'}$), 4.49 (1H, m, $H_{5'}$), 3.83 (1H, dd, H_{3a}), 3.60

(1H, d, J = 11.4 Hz, H_{3b}), 2.50 (1H, m, H_4), 1.95 and 1.72 (2H, 2dd, $-CH_2-$ side chain), 1.58 (2H, m, $-CH_2-$ sugar), 1.31 (3H, d, J = 6.4 Hz, $-CH_3$ sugar), 0.92 (3H, t, J = 7.3 Hz, $-CH_3$ side chain).

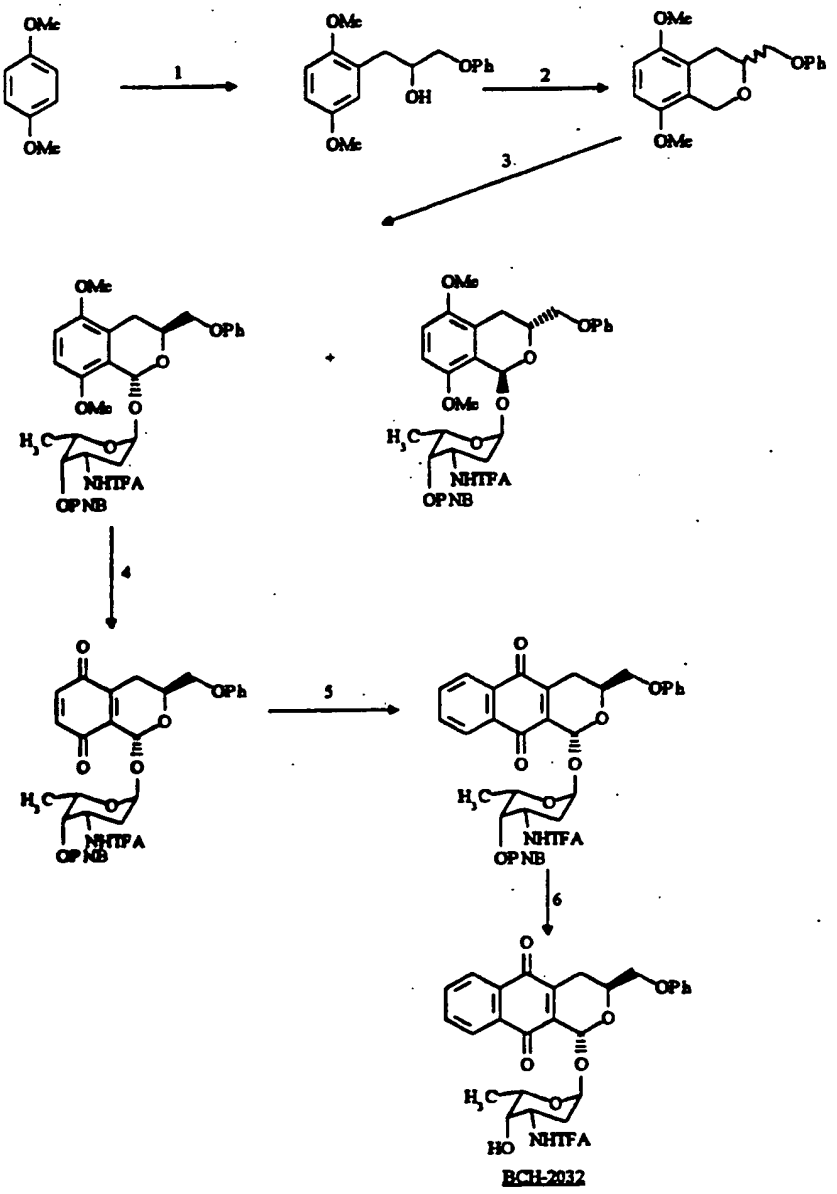
Step 7: (1'S, 1R, 4R)-5,10-dioxo-4-ethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c] pyran (BCH-2091)

The titled compound was obtained via deprotection of the tricyclic glycoside from step 6 herein as per procedure from step 6, example 34.

NMR ^1H (250 MHz) ($CDCl_3$; ppm): 8.10 (2H, m, aromatics), 7.75 (2H, m, aromatics), 6.72 (1H, d, NH), 5.91 (1H, s, H_1), 5.41 (1H, s, $H_{1'}$), 4.59 (1H, q, J = 6.6 Hz, $H_{5'}$), 4.46 (1H, m, $H_{4'}$), 4.32 (1H, m, $H_{3'}$), 4.03 (1H, dd, J_1 = 3.0 Hz, J_2 = 11.6 Hz, H_{3a}), 3.85 (1H, d, J = 11.6 Hz, H_{3b}), 3.64 (1H, m, OH), 2.66 (1H, m, H_4), 1.99 (1H, d, J = 8.3 Hz, $-CH_2-$ side chain), 1.86 (2H, m, $H_{2'a}$ and $-CH_2-$ side chain), 1.65 (1H, m, $H_{2'b}$), 1.41 (3H, d, J = 6.5 Hz, $-CH_3$ sugar), 1.06 (3H, t, J = 7.3 Hz, $-CH_3$ side chain).

IR (film) (cm^{-1}): 3422 (OH), 2932 (CH aliphatic), 1710 (C=O), 1668 (C=C), 1299 and 1165 (C-O).

Example 36: **Preparation of (1'S,1R,3S)-5,10-dioxo-3-phenyloxymethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c] pyran**



Step 1: **α-phenoxymethyl-2,5-dimethoxy-phenetyl alcohol**

To a solution of 1,4-dimethoxybenzene (2.0 g; 14.5 mmol) in tetrahydrofuran at 0°C was added n-butyl-lithium (2.5 M in hexane; 5.8 ml; 14.5 mmol). The mixture was warmed to room temperature and stirred for 4 hours. It was then cooled to -78°C and 1,2 epoxy-3-phenoxy-propane (1.95 g; 13 mmol) was added followed by boron trifluoride etherate (1.85 g; 13 mmol). The resulting mixture was stirred at -78°C for 2 hours. It was quenched with saturated $NaHCO_3$ solution and extracted with

dichloromethane. The combined organic layers were washed with bicarbonate, brine and were dried over $MgSO_4$. The crude residue was purified by column chromatography on silica gel using 25% ethyl acetate in hexane to yield the title product (2.4 g; 64%).

^1H NMR (250 MHz, $CDCl_3$) δ: 2.75 (1H, d, J = 4 Hz, -OH), 2.85-3.10 (2H, m, Ar-CH_2-), 3.71 (3H, s, OCH_3), 3.79 (3H, s, OCH_3), 3.95 (2H, m, CH_2-O), 4.29 (1H, m, -CH-O), 6.70-7.00 (6H, m, Ar-H), 7.28 (2H, m, Ar-H).

Step 2: **5,8-dimethoxy-3-phenoxymethyl-isochroman**

To a solution of α-phenoxymethyl-2,5-dimethoxyphenetyl alcohol (2.1 g; 7.24 mmol) in ether (40 ml) at room temperature was added dimethoxymethane (966 µl; 10.8 mmol) and then boron trifluoride etherate (2.68 ml; 21.6 mmol). The rest of the procedure is identical to the second part, step 1, example 29, to yield the title product (715 mg; 33%).

^1H NMR (250 MHz, $CDCl_3$) δ: 2.65 (1H, dd, J = 11 and 17 Hz, H-4 ax), 2.89 (1H, dd, J = 2 and 17 Hz, H-4 eq), 3.79 (3H, s, -OCH_3), 3.82 (3H, s, -OCH_3), 4.00-4.30 (3H, m, -CH_2-OPh and H-3), 4.73 (1H, d, J = 16 Hz, H-1), 5.07 (1H, d, J = 16 Hz, H-1), 6.68 (2H, AB doublets, Ar-H), 7.01 (3H, m, Ar-H), 7.33 (2H, m, Ar-H).

Step 3: **(1'S, 1R, 3S)-5,8-dimethoxy-3-phenyloxymethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-isochroman**

The isochroman from step 3 herein was glycosydated in 57% yield as per procedure described in step 3, example 34.

NMR ^1H (250 MHz) ($CDCl_3$; ppm): 8.31 (4H, m, aromatics), 7.31 (2H, m, aromatics), 6.97 (3H, m, aromatics), 6.76 (2H, m, aromatics), 6.22 (1H, d, NH), 6.02 (1H, s, H_1), 5.63 (1H, s, $H_{1'}$), 5.42 (1H, s, $H_{3'}$), 4.67 (1H, m, $H_{4'}$), 4.66 (1H, m, $H_{5'}$), 4.57 (1H, m, H_3), 4.18 (2H, m, -CH_2- side chain), 3.82 (3H, s, OCH_3), 3.81 (3H, s, OCH_3), 2.90 (1H, dd, H_{4a}), 2.56 (1H, dd, H_{4b}), 2.00-2.18 (2H, m, -CH_2- sugar), 1.16 (3H, d, J = 6.5 Hz, -CH_3 sugar).

Step 4: **(1'S, 1R, 3S)-5,8-dioxo-3-phenyloxymethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-isochroman**

The (1'S,1R,3S) glycoside from step 3 herein was oxidatively demethylated as per procedure described in step 4, example 34.

NMR ^1H (250 MHz) (C_6D_6; ppm): 7.73 (4H, dd, aromatics), 7.17 (2H, m, aromatics), 6.90 (3H, d, aromatics), 6.71 (1H, d, NH), 6.08 (2H, d, quinone ring), 5.80 (1H, s, H_1), 5.76 (1H, s, $H_{1'}$), 5.50 (1H, s, $H_{3'}$), 4.70 (1H, m, $H_{4'}$), 4.62 (1H, m, $H_{5'}$), 4.22 (1H, m, H_3), 3.85 (1H, m, CH_2 side chain), 3.66 (1H, dd, CH_2 side chain), 2.27 (1H, dd, H_{4a}), 1.94 (1H, dd, H_{4b}), 1.85 (2H, m, -CH_2 side chain), 1.34 (2H, m, -CH_2- sugar), 1.18 (3H, d, -CH_3 sugar).

Step 5: **(1'S, 1R, 3S)-5,10-dioxo-3-phenyloxymethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c] pyran**

Cycloaddition between 1-acetoxybutadiene and the quinone from step 4 herein as per procedure described in step 5, example 34, afforded the titled compound, yield 148%.

NMR ^1H (250 MHz) ($CDCl_3$; ppm): 8.30 (3H, m, aromatics), 8.11 (2H, m, aromatics), 7.77 (2H, m, aromatics), 7.30 (4H, m, aromatics), 6.96 (2H, m, aromatics), 6.40 (1H, d, J = 7.5 Hz, NH), 6.01 (1H, s, H_1), 5.75 (1H, s, $H_{1'}$), 5.43 (1H, s, $H_{3'}$), 4.63 (1H, m, $H_{4'}$), 4.61 (1H, m, H_3), 4.60 (1H, m, $H_{5'}$), 4.20 (2H, m, $-CH_2-$ side chain), 2.89 (1H, dd, J_1 = 3.4 Hz, J_2 = 19.3 Hz, H_{4a}), 2.57 (1H, dd, J_1 = 11.5 Hz, J_2 = 19.4 Hz, H_{4b}), 2.07 (2H, dd, $-CH_2-$ sugar), 1.19 (3H, d, J = 6.5 Hz, $-CH_3$ sugar).

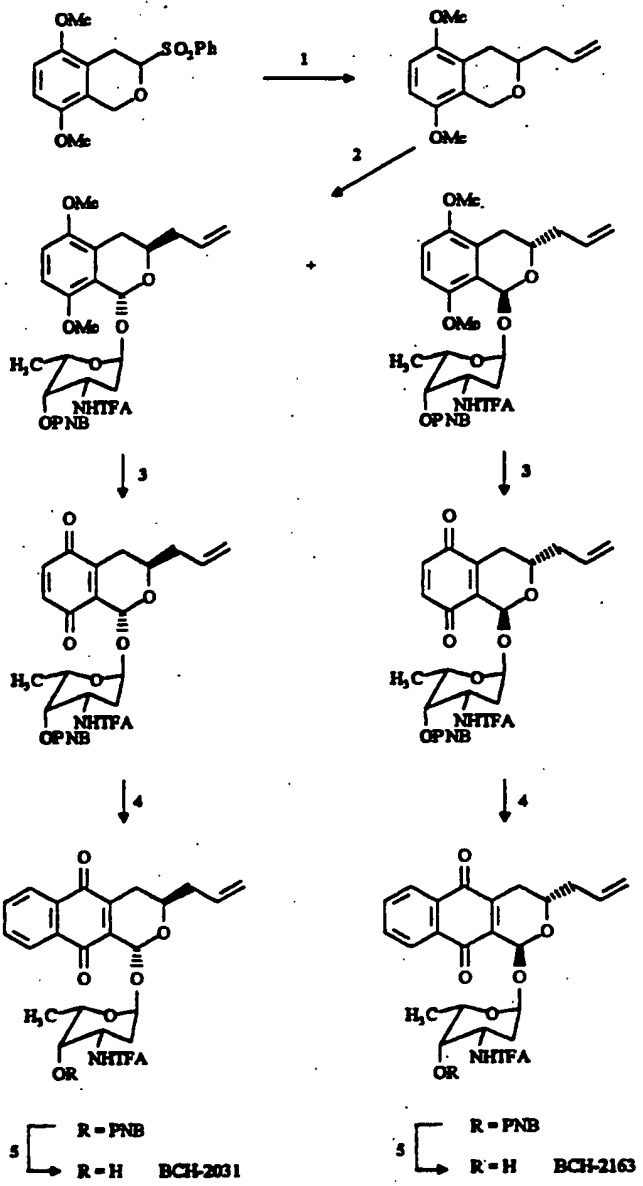
Step 6: **(1'S, 1R, 3S)-5,10-dioxo-3-phenyloxymethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c] pyran (BCH-2032)**

The glycoside from step 5 herein was deprotected as per procedure described in step 6, example 34, to afford the titled compound in 81% yield.

NMR ^1H (250 MHz) $CDCl_3$; ppm): 8.11 (2H, m, aromatics), 7.78 (2H, m, aromatics), 7.33 (2H, m, aromatics), 6.98 (1H, m, aromatic), 6.91 (2H, d, J = 8.3 Hz, aromatics), 6.69 (1H, d, NH), 5.95 (1H, s, H_1), 5.55 (1H, d, $H_{1'}$), 4.61 (1H, m, $H_{4'}$), 4.41 (1H, m, $H_{5'}$), 4.38 (1H, m, H_3), 4.16 (2H, m, $-CH_2-$ side chain), 3.64 (1H, m, OH), 2.89 (1H, dd, H_{4a}), 2.57 (1H, dd, H_{4b}), 1.93 (2H, m, $-CH_2-$ sugar), 1.24 (3H, d, J = 6.5 Hz, $-CH_3$ sugar).

IR (film) (cm^{-1}): 3425 (OH, NH), 2929 (Ch aliphatic), 1716 (C=O), 1668 (C=C), 1596 (C-N), 1297 and 1160 (C-O).

Example 37: **Preparation of naphtho-[2,3-c] pyran derivatives with an allyl side chain**



Step 1: **5,8-dimethoxy-3-(2-propenyl)-isochroman**

To a stirred solution of pyranosulfone (670 mg, 2.0 mmol) in CH_2Cl_2 (20 ml) at -78°C were added allyltrimethylsilane (636 µl, 4.0 mmol) and $AlCl_3$ (533 mg, 4.0 mmol). Temperature was then raised to -35°C few minutes, then HCl (0.1 N, 10 ml) was added. The reaction mixture was worked up with CH_2Cl_2 and water. The organic layer was washed with brine and dried over $MgSO_4$. The solvent was evaporated to give the allyl isochroman (450 mg, 96%).

^1H NMR (250 MHz, $CDCl_3$) δ: 6.63 (2d, J = 8.9 Hz, 2H, Ar-H), 5.96 (m, 1H, -CH=C), 5.17 (d, J = 17 Hz, 1H, -CH=CH_2), 5.10 (d, J = 9.9 Hz, 1H, -CH=CH_2), 4.93 (d, J = 16.0 Hz, 1H, H-1), 4.58 (d, J = 16.0 Hz, 1H, H-1), 3.78 and 3.75 (2s, 6H, 2xOCH_3), 3.65 (m, 1H, H-3), 2.75 (broad d, J = 17.0 Hz, 1H, H-4), 2.45 (m, 3H, H-4, -CH_2-CH=C).

Step 2: (1'S,1S,3S) and (1'S,1-R,3-R)-1-(2',3',6',-trideoxy-3'-trifluoroacetamido-4'-O-paranitrobenzoyl-L-lyxohexopyranose)-5,8-dimethoxy-3-(2-propenyl)-isochroman

To a mixture of 5,8-dimethoxy-3-(2-propenyl)-isochroman (400 mg, 1.72 mmol), 2',3',6'-trideoxy-3-trifluoroacetamido-4-O-paranitrobenzoyl-1-α,β-hydroxy-lyxohexopyranose 2 (1.2 eq., 810 mg, 2.06 mmol) and MS4Å (500 mg) in CH_2Cl_2 (17 ml) at room temperature was added DDQ (1.5 aq., 586 mg, 2.58 mmol). The reaction mixture was stirred for 3 hours and 30 minutes, then filtered and the filtrate was washed by extraction with $NaHCO_3$ sat. solution. Evaporation of the solvent and purifying by FC (CH_2Cl_2:Hex:EtOAc 8:12:1) gave 427 mg of the titled product (50%) and 531 mg of its diastereoisomer (50%). The (1'S,1S,3S) diastereomer was prepared using the same procedure.
^1H NMR (250 MHz, acetone-d_6) δ (ppm): 8.65 (bd,1H,NH), 8.4 (d,8.9Hz,2H,PNB-H), 8.34 (d,8.9Hz,2H, PNB-H), 6.86 (d,8.8Hz,1H,Ar-H), 6.8 (d,8.8Hz,1H,Ar-H), 6.0 (m,1H,C=CH-C), 5.88 (s,1H,H-1), 5.56 (bs, 1H,H-1'), 5.47 (bs,1H,H-4'), 5.14 (bm,2H,C=CH_2), 4.6 (m,2H,H-3',H-5'), 4.3 (m,1H,H-3), 3.8 (s,3H,A$COCH_3$), 3.78 (s,3H,Ar-OCH_3), 2.75 (m,1H,H-4), 2.47 (m,2H,C=C-CH_2), 2.4 (m,1H,H-4), 2.3 (m,1H,H-2'), 1.9 (m,1H,H-2'), 1.16 (d,6.4Hz,3H,H-6').

Step 3: (±)-Methyl ketone hydroxy-1-isochroman quinone

To a stirred solution of the methyl ketone hydroxy-1 isochromane (3.000g, 11.891mmol) in 180ml of acetonitrile at 0°C was added dropwise an aqueous solution of CAN (26.076g, 47.56 mmol) and NaHCO3 (7.19g, 85.6 mmol) in water. The reaction mixture was then droped in a mixture of 200 ml of CH_2Cl_2 and 200 ml of water and extracted with CH_2Cl_2 and back extracted with Ethyl Acetate. Combined organic layers were washed with water (3x300 ml)and then dried (Na_2SO_4). Recristallisation of the residu gave 2.237g (85% yield) of the pure methyl ketone hydroxy-1 isochromane quinone.
PMR ($CDCl_3$, 300MHz)δ: 2.30 (s, 3H, $COCH_3$), 2.39 (ddd, 1H, J = 20.0 Hz, 12.0 Hz and 1.2 Hz, CH_aCHCO), 2.88 (dd, 1H, J = 19.5 Hz and 3.9 Hz, CH_eCHCO), 3.42 (broad m, 1H, OH-1), 4.64 (dd, 1H, J = 11.7 Hz and 4 Hz, H-3), 6.03 (broad s, 1H, H-1), 6.78 (2xd, 2H, quinone-H).

Step 4: (1'S,1S,3S) and (1'-S,1-R,3-R)-3-([2',3',6'-trideoxy-3'-trifluoroacetamidoo-4'-paramitrobenzoyl-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-c]-pyran-3-yl)-propene

To a solution of (1,-S,1-R,3-R)-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-paranitrobenzoyl-L-lyxohexopyranose)- 5,8-dioxo-3-propenyl-1,4,5,8-tetrahydrobenzo-[2,3-c]-pyran (205 mg, .34 mmol) in

toluene (10 ml) at room temperature was added 1-acetoxy-1,3-butadiene (0.250 ml, 1.72 mmol). The mixture was stirred overnight followed by adding silica gel (4.2 g) and bubbling air. After 2 hours, the solution was filtered and solvent removed form the filtrate. Purifying of the crude by FC (Tol.: EtOAc 15:1) and recrystalization gave 133 mg of the titled product. The (1'S,1S,3S) diastereomer was prepared the same way.

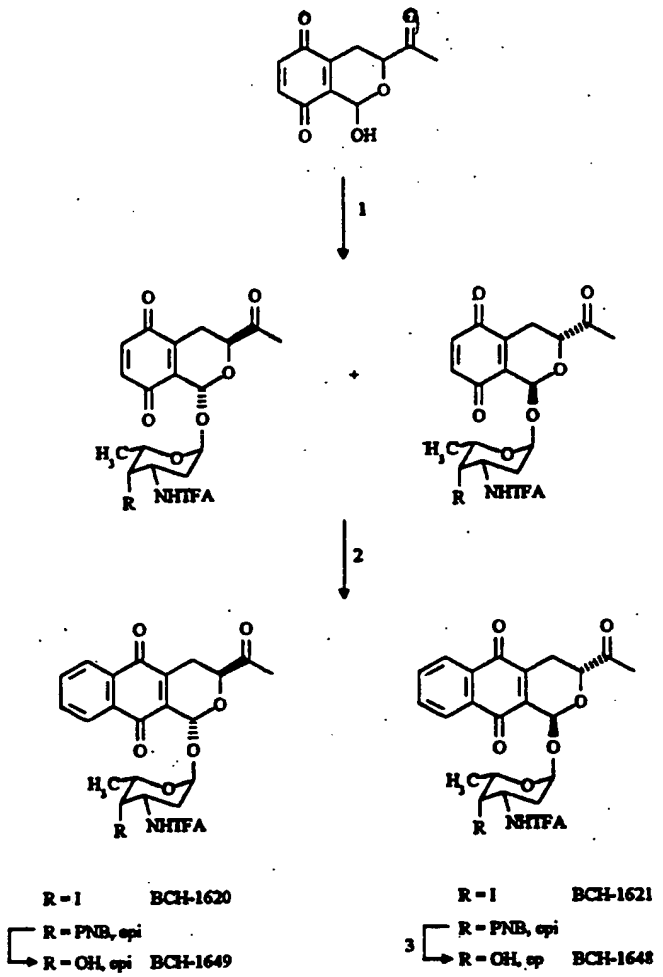
^{1}H NMR (250 MHz, CD_2Cl_2) δ (ppm): 8.3 (m,4H,PNB-H), 8.1 (m,2H,Ar-H), 7.75 (m,2H,Ar-H), 6.35 (bd,1H,NH), 5.95 (1H,C=CH-C), 5.9 (s,1H,H-1), 5.7 (s,1H,H-1'), 5.43 (bs,1H,H-4') , 5.25 (m,2H,C=CH_2), 4.6 (m,1H,H-3'), 4.43 (q,6.4Hz,1H,H-5'), 4.21 (m,1H,H-3), 2.8 (dd,19.4Hz,3.2Hz,1H,H-4), 2.47 (m,2H,C=C-CH_2), 2.33 (dd,19.4Hz, 11Hz,1H,H-4), 2.07 (m,2H,H-2'), 1.2 (d,6.4Hz,3H,H-6').

Step 5: **(1'S,1S,3S) and (1'S,1-R,3-R)-3-([2',3',6'-trideoxy-3'-trifluoroacetamido-4'-hydroxy-L-lyhohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-c]-pyran-3-yl)-propene (BCH-2031)**

To a solution of (1'-S,1-R,3-R)-3-([2',3',6'-trideoxy-3'-trifluoroacetamido-4'-paranitrobenzoyl-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-c]-pyran-3-yl] propene (133 mg, 0.2 mmol) in MeOH (2 ml) at 0°C was added NaOMe (4.37M in MeOH, 60µl, .26 mmol) and stirred for 15 minutes. The reaction was quenched by adding NH_4Cl sat. and extracted with CH_2Cl_2. The organic phase was then dried over $MgSO_4$, evaporated to give 64 mg crude. Purifying by preparative TLC (Tol.: EtOAc 6:1) gave 25 mg (25%) of the desired product. The (1'S,1S,3S) diastereomer BCH-2163 was prepared the same way.

^{1}H-NMR (250MHz,CD_2Cl_2) δ (ppm): 8.05 (m,2H,Ar-H), 7.75 (m,2H,Ar-H), 6.25 (bd,1H,NH), 5.95 (m, 1H,C=CH), 5.84 (s,1H,H-1), 5.51 (bd,1H,H-1'), 5.2 (m,2H,C=CH_2), 4.25 (m,4H,H-3,3',4',5'), 3.6 (bs, 1H,OH), 2.78 (dd,19.4Hz,3.3Hz,1H,H-4), 2.44 (m,2H,C=C-CH_2), 2.3 (dd,19.4Hz,11Hz,1H,H-4), 1.85 (m,2H,H-2'), 1.25 (d,6.6Hz,3H,H-6').

Example 38: **Preparation of naphtho-[2,3-c] pyran derivatives with a methyl ketone side chain from a bicyclic quinone aglycal**



Step 1 and 2: **(1'-S,1-R,3-S)-methyl-(1-[2',3',6'-trideoxy-3'-trifluoroacetamido-4'-iodo-L-lyxohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-c]-pyran-3-yl)-ketone (BCH-1620)**

1) To a stirred suspension of molecular sieves 4Å (1.3g), 2-(dimethyl-t-butyl-silyloxy)-3-acetamido-4-iodo-2,3,6-trideoxy-α, β-L-lyxohexopyranose (478 mg, 1.02 mmol) and 3-acetyl-5,8-dioxo-1-hydroxy-1,4,5,8-tetrahydrobenzo-[2,3-c]-pyran (178 mg, 0.8 mmol) in a solution of CH_2Cl_2/acetone (15.4 ml, 10:1) at -50°C was added trimethylsilyl trifluoromethanesulfonate (TMS-OTf, .222 ml, 1.15 mmol). The reaction mixture was then stirred at -30°C for 50 minutes, followed by addition of aq. $NaHCO_3$ 5% and warmed up to room temperature. After filtering off solids, the filtrate was extracted with CH_2Cl_2. The organic phase was then washed with brine and dried over $MgSO_4$. Evaporation of the solvent gave 563 mg of the crude.

2) From the crude product obtained as described above, 116 mg was utilized in the next step by stirring with 1-acetoxy-1,3-butadiene (98 µl, .82 mmol) in toluene (10 ml) for overnight at room temperature and under argon. Silica gel was next added and air was bubbled into the reaction mixture and stirring for 2 hours. The crude product was recovered by filtering and washing of

the silica gel with ethyl acetate. Evaporation of the solvent gave 139 mg of the crude product. Purifying by preparative TLC (hex:OAc 4:1) gave 7.4 mg of the title product and 2.2 mg of its diastereoisomer for a total of 9% yield. The (1'S,1S,3R) diastereomer BCH-1621 was prepared using the same method.

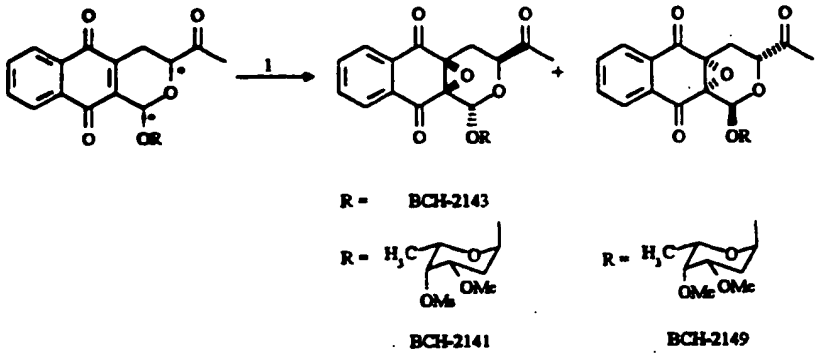
^{1}H NMR (250 MHz, acetone) δ (ppm): 8.43 (bd,1H,N-H), 8.0 (m,2H,ArH), 7.9 (m,2H,Ar-H), 6.0 (s,1H, H-1), 5.6 (bd, 5.4Hz,1H,H-1'), 4.89 (bs,1H,H-3'), 4.75 (dd,11.6Hz,4.0Hz,1H,H-3), 3.75 (m,1H,H-4'), 3.7 (q,6.1Hz,1H,H-5'), 3.0 (dd,19.6Hz,4Hz,1H,H-4), 2.55 (dd,19.6Hz,11.6Hz,1H,H-4), 2.3 (s,3H,$COCH_3$), 2.26 (m,1H,H-2'), 1.8 (m,1H,H-2'), 1.25 (d,6.1Hz,3H,H-6').

Step 3: **(1'-S,1-R,3-S)-3-([2',3',6'-trideoxy-3'-trifluoroacetamido-4'-hydroxy-L-lyhohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-c]-pyran-3-yl)-propene (BCH-1649)**

To a solution of (1'-S,1-R,3-S)-3-([2',3',6'-trideoxy-3'-trifluoroacetamido-4'-paranitrobenzoyl-L-lyxohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-c]-pyran-3-yl) propene (133 mg, 0.2 mmol) in MeOH (2 ml) at 0°C was added NaOMe (4.37M in MeOH, 60 µl, .26 mmol) and stirred for 15 minutes. The reaction was quenched by adding NH_4Cl sat. and extracted with CH_2Cl_2. The organic phase was then dried over $MgSO_4$, evaporated to give 64 mg crude. Purifying by preparative TLC (tol: EtOAc 6:1) gave 25 mg (25%) of the desired product. The (1'S,1S,3R), BCH-1648, diastereomer was obtained using the same method.

^{1}H NMR (250MHz,CD_2Cl_2) δ (ppm): 8.05 (m,2H,Ar-H), 7.75 (m,2H,Ar-H), 6.25 (bd,1H,NH), 5.95 (m, 1H,C=CH), 5.84 (s,1H,H-1), 5.51 (bd,1H,H-1'), 5.2 (m,2H,$C=CH_2$), 4.25 (m,4H,H-3,3',4',5'), 3.6 (bs, 1H,OH), 2.78 (dd,19.4Hz,3.3Hz,1H,H-4), 2.44 (m,2H,$C=C-CH_2$), 2.3 (dd,19.4Hz,11Hz,1H,H-4), 1.85 (m,2H,H-2'), 1.25 (d,6.6Hz,3H,H-6').

Example 39: Preparation of 4a,10a-epoxy-naphtho-[2,3-c] pyran derivatives

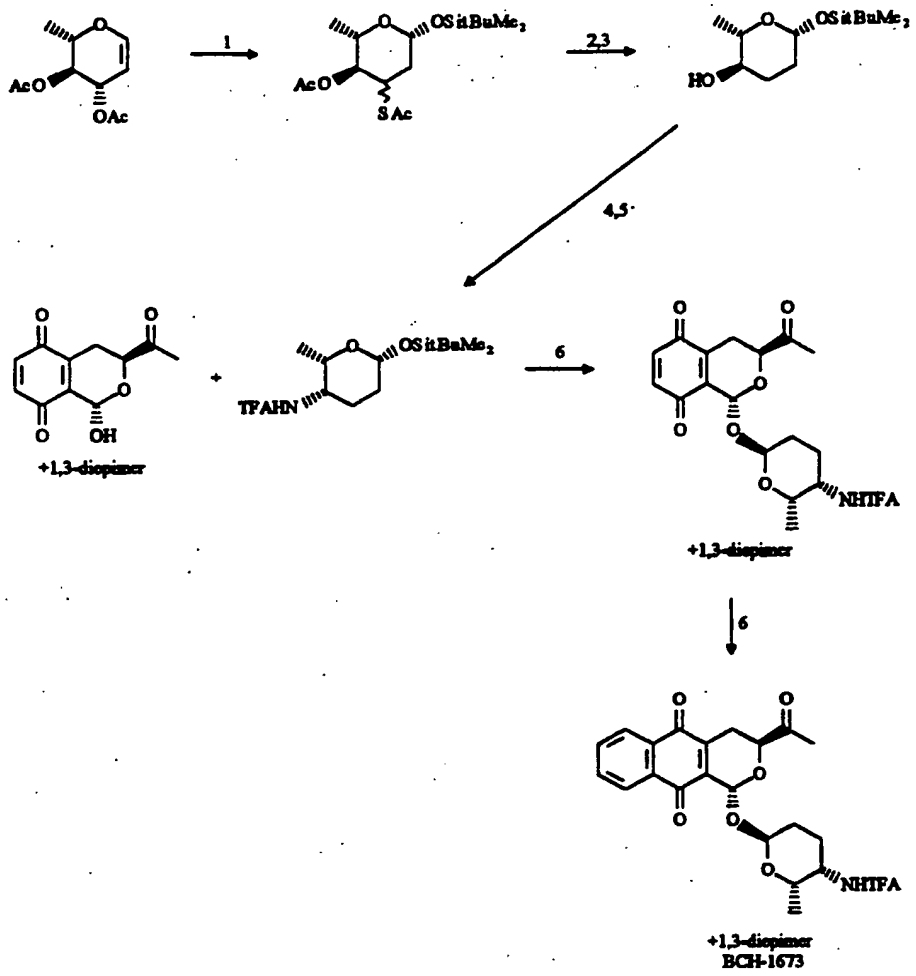


Step 1: **(1'-S,1-R,3-S,4a-S,10a-S)-methyl-(1-[2',3',4',6'-tetradeoxy-3'-methoxy-4'-O-methanesulfonyl-L-lyxohexopyranose)-4a,10a-epoxy-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-c] pyran-3-yl) ketone (BCH-2141)**

To a solution of (1'-S,1-R,3-S)-methyl-(1-[2',3',4',6'-tetradeoxy-3'-methoxy-4'-O-methansulfonyl-L-lyxohexopyranose)-5,10-dioxo-3,4-dihydronaphtho-[2,3-c] pyran-3-yl) ketone (15 mg, 30 µmol) in THF (1 ml) at 0°C was added H_2O_2 (30% aq. solution , 5.2 µl, 46 µmol). After 10 minutes, NaOH (.1N, .364 ml) was added and the reaction mixture was stirred at 0°C for 30 minutes. Workup was carried out by adding brine to the mixture, extracting with CH_2Cl_2 and drying the organic phase over $MgSO_4$. The crude obtained after evaporation of the solvent was purifying by recrystalization to give 8 mg (50%) of the pure titled product. The (1'S,1S,3R,4aR,10aR), BCH-2149, diastereomer was obtained using the same method

^1H NMR (250MHz, $CDCl_3$) δ (ppm): 8.05 and 7.8 (m,4H,ArH), 6.15 (s,1H,H-1), 5.55 (bd,1H,H-1'), 4.86 (bs,1H,H-4'), 4.3 (dd,9Hz,3Hz,1H,H-3), 4.05 (q,6.6Hz,1H,H-5'), 3.65 (m,1H,H-3'), 3.45 (s,3H,SO_2CH_3), 3.15 (s,3H,OMe), 2.75 (dd,12.3Hz,3Hz,1H,H-4), 2.35 (m,1H,H-4), 2.3 (s,3H,$COCH_3$), 1.9-2.2 (m,2H,H-2'), 1.25 (d,6.6Hz,3H,H-6').

Example 40: **Monoaminosugar substituted naphthoquinone derivative**



Step 1: **(2R,4R,5S,6S) and (2R,4S,5S,6S)-2-tert-butyldimethylsilyloxy-4-thioacetoxy-5-acetoxy-6-methyl-tetrahydropyran**

A solution of rhamnal diacetate (0.514 g, 2.4 mmols) in H_2O (24 ml) is heated at 80°C for 30 minutes. The solution is then cooled down to 0°C and CH_3COSH (0.51 ml, 3 eq.) is then added. The cloudy solution is stirred at room temperature for 2 hours after which $NaHCO_3$ (1.2 g, 6 eq.) is added to neutralize the excess CH_3COSH. The water is evaporated and the residue is dissolved in CH_2Cl_2 and dried over $MgSO_4$. The solids are filtered and the solvent evaporated. A solution of the oil obtained after evaporation in CH_2Cl_2 (24 ml) is treated with imidazole (0.33 g, 2 eq.) and t-$BuMe_2SiCl$ (0.43 g, 1.2 eq.). The solution is stirred at room temperature, under argon, for 18 hours. It is poured in sat. aq. $NaHCO_3$ and the phases are separated. The aqueous layer is extracted with CH_2Cl_2 (2x) and the combined organic extracts are dried over $MgSO_4$. The solids are filtered and the solvents evaporated.

The oil obtained is purified by flash chromatography (silica gel, 9:1 hexanes/EtOAc) to give a 1:1 mixture of titled isomers: 0.50 g (60%) as a clear oil.

^{1}H NMR ($CDCl_3$): δ 4.90+4.85 (2dd, 1H, H-1), 4.73+4.62 (2dd, 1H, H-4), 4.30+3.75 (q+m, 1H, H-5), 3.71+3.55 (2ddd, 1H, H-3), 2.36+2.30 (2s, 3H, SAc), 2.19 (m, 1H, H-2), 2.03+1.99 (2s, 3H, OAc), 1.77 (m, 1H, H-2), 1.22+1.18 (2d, 3H, H-6), 0.88 (s, 9H, t-Bu), 0.09+0.10 (2s, 6H, $SiMe_2$).

Step 2: (2R,5R,6S)-2-tert-butyldimethylsilyloxy-5-acetoxy-6-methyl-tetrahydropyran

A solution of the thio-sugar from step 1 herein (51 mg, 0.14 mmol) in ethanol (2 ml) was treated with an excess of Raney-Ni. The suspension was vigorously stirred for 30 minutes and was then filtered through Celite. The ethanol was evaporated to give 36 mg (89%) of the titled compound as a clear oil.

^{1}H NMR ($CDCl_3$): δ 4.74 (dd, 1H, J = 2.0, 8.6, H-1), 4.42 (ddd, 1H, J = 4.7, 10.5, 10.5, H-4), 3.98 (dq, 1H, J = 6.16, 9.23, H-5) 2.10 (m, 1H, H-2 or H-3), 2.02 (s, 3H, OAc), 1.86-1.35 (m, 3H, H-2 and H-3), 1.17 (d, 3H, J = 6.16, H-6), 0.88 (s, 9H, t-Bu), 0.10 (s, 3H, SiMe), 0.08 (s, 3H, SiMe).

Step 3: (2R,5R,6S)-2-tert-butyldimethylsilyloxy-5-hydroxy-6-methyl-tetrahydropyran

To a solution of the acetate from step 2 herein (36 mg, 0.13 mmol) in dry MeOH (1.3 ml), at room temperature, was added 1 N NaOH (0.14 ml, 1.1 eq.) and the solution was stirred for 45 minutes. It was then poured in H_2O and the aqueous phase was extracted 3x with CH_2Cl_2. The combined organic extracts were dried over $MgSO_4$, the solids were filtered and the solvent evaporated to give 30 mg (96%) of the pure titled alcohol.

^{1}H NMR ($CDCl_3$): δ 4.72 (dd, 1H, J = 1.9, 8.7, H-1), 3.28-3.24 (m, 2H, H-4 and H-5), 2.04-1.41 (m, 4H, H-2 and H-3), 1.27 (d, 3H, J = 5.5, H-6), 0.88 (s, 9H, t-Bu), 0.10 (s, 3H, SiMe), 0.09 (s, 3H, SiMe).

Step 4: (2R,5S,6S)-2-tert-butyldimethylsilyloxy-5-azido-6-methyl-tetrahydropyran

To a solution of the alcohol from step 3 herein (62 mg, 0.25 mmol) in dry THF (2.5 ml), at room temperature, under argon, were added successively Ph_3P (66 mg, 1 eq.), DEAD (40 µl, 1 eq.) and $(PhO)_2PON_3$ (54 µl, 1 eq.) and the solution was stirred for 18 hours. The THF was evaporated and the crude oil was purified by flash chromatography (silica gel, 95:5 hexanes/EtOAc) to give 38 mg (56%) of the titled azide as a clear oil.

^{1}H NMR ($CDCl_3$): δ 4.71 (dd, 1H, J = 3.0, 7.9, H-1), 3.64 (dq, 1H, J = 1.7, 6.3, H-5), 3.33 (m, 1H, H-4), 2.15-1.60 (m, 4H, H-2 and H-3), 1.26 (d, 3H, J = 6.3, H-6), 0.89 (s, 9H, tBu), 0.11 (s, 3H, SiMe), 0.09 (s, 3H, SiMe).

Step 5: (2R,5S,6S)-2-tert-butyldimethylsilyloxy-5-trifluoroacetamido-6-methyl-tetrahydropyran

To a solution of the azide from step 4 herein (0.20 g, 0.72 mmol) in dry EtOAc (7.2 ml) at room temperature, was added Pd/C 10% (0.10 g, 50% wt.) and the black suspension was placed under a H_2 atmosphere for 3 hours. The catalyst was then filtered through Celite and the solvent was evaporated to dryness. The crude amine (0.18 g, 0.72 mmol) was dissolved in dry CH_2Cl_2 (7.2 ml) and Et_3N (0.20 ml, 2 eq.) was added. The solution was cooled to 0°C and TFA_2O (0.11 ml, 1.1 eq.) was added slowly. The solution was stirred at 0°C for 5 hours and was then poured in sat. aq. $NaHCO_3$. The phases were separated and the aqueous layer was extracted with CH_2Cl_2 (2x). The combined organic extracts were dried over $MgSO_4$, the solids filtered and the solvent evaporated to give 0.17 g (71%) of the crude titled trifluoroacetamide that was used as such.

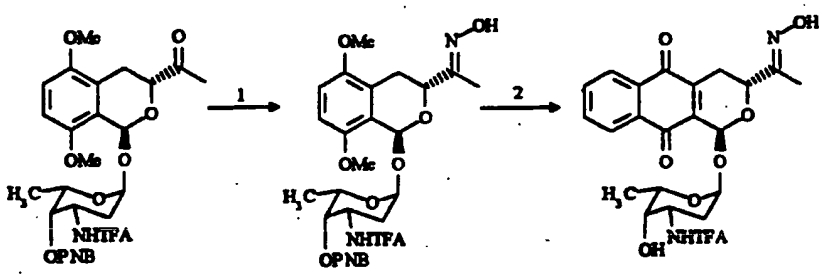
^1H NMR ($CDCl_3$): δ 6.70 (bs, 1H, NH), 4.75 (dd, 1H, H-1), 3.92 (m, 1H, H-4), 3.73 (dq, 1H, H-5), 2.06-1.45 (m, 4H, H-2 and H-3), 1.19 (d, 3H, H-6), 0.88 (s, 9H, t-Bu), 0.11 (s, 3H, SiMe), 0.09 (s, 3H, SiMe).

Step 6: (1S,3R,1'S,5'S,6'S) and (1R,3S,1'S,5'S,6'S)-methyl-(1-[4'trifluoroacetamido-5'-methyltetrahydropyranyl]-5,10-dioxo-3,4,5,10-tetrahydronaphthaleno-[2,3-c] pyran-3-yl) ketone (BCH-1673)

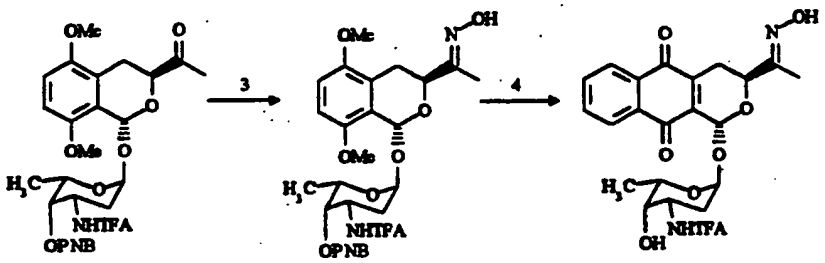
The titled compounds were obtained in 30% yield by following the procedure described in step 4, example 12, on the precursor of step 5 herein. The titled compounds were purified via flash chromatography (silica gel, 3:1 hexanes/EtOAc). The mixture of isomers was not separable by chromatography.

^1H NMR ($CDCl_3$): δ 8.14-8.07 (m, 2H, ArH), 7.79-7.73 (m, 2H, ArH), 6.17+5.99 (2s, 1H, H-1), 5.50+5.39 (2bs, 1H, H-1'), 4.68+4.24 (2q, 1H, J = 6.5, H-5'), 4.56+4.49 (2dd, 1H, J = 4.2, 11.8, H-3), 4.05 (m, 1H, H-4'), 3.08+3.07 (2dd, 1H, J = 4.2, 19.9, H-4), 2.57 (dd, 1H, J = 11.8, 19.9, H-4), 2.34+2.33 (2s, 3H, $COCH_3$), 2.00-1.53 (m, 4H, H-2' and H-3'), 1.31+1.13 (2d, 3H, J = 6.5, H-6').

Example 41: (1'S,1S,3R)-3-(oximoethyl)-5,10-dioxo-1(2,3,6-trideoxy-3-trifluoroacetamido-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho [2,3-c] pyran (BCH-2101) and 1,3-diepimer (BCH-2115)



BCH-2101



BCH-2115

Step 1: (1S,3R)-3 (oximoethyl)-1 (2,3,6-trideoxy-3-trifluoroacetamido-4-p-nitrobenzoyl-L-lyxohexopyranose)-5,8-dimethoxy-isochroman

To a solution of hydroxylamine-hydrochloride (60 mg; .86 mmol) in a mixture of ethanol (4 ml) and water (.4 ml) was added sodium hydroxide (33 mg) in ethanol (2 ml). The mixture was stirred at room temperature for .5 hour. The solution was filtered. The filtrate was added to 3-acetyl-isochroman glycoside from step 1, example 5, (92 mg; .147 mmole). The reaction was complete in 10 minutes. The mixture was evaporated down to dryness, dissolved in small volume of water (5 ml), extracted with CH_2Cl_2 (3x50 ml), washed with sat. NaCl, dried and evaporated. The crude product was passed through a small column of silica gel prewashed with 0.2% triethylamine in hexane (eluent: 15%, 20% and 25% EtOAc in hexane) yielding pure oxime (63 mg; 67%).

NMR (acetone-d_6; δ): 1.26 (3H, d, J = 6.8 Hz; $-CH_3$), 1.26 (3H, d, J = 8.3 Hz; $-CH_3$), 1.89 (1H, dd, J = 4.4, 13.2 Hz; H-2 of the sugar), 1.96 (3H, s, CH_3 of the side chain), 2.47 (1H, dt, J = 3.6, 13.1 Hz; H-2), 3.81, 3.88 (3H, s each; Ar-OCH_3), 4.60-4.66 (1H, m; sugar-H), 4.72 (1H, t, J = 7.8 Hz; H-3), 4.83 (1H, q; J = 6.5 Hz; H-5 of the sugar), 5.51 (1H, br singlet; H-1 of the sugar), 5.61 (1H, d, J = 2.9 Hz; H-4 of the sugar), 6.15 (1H, s; H-1), 6.87, 6.90 (1H, d each; J = 8.9 Hz; Ar-H), 8.36, 8.41 (2H, d each; J = 8.8 Hz; Ar-H of PNB-group), 8.70 (1H, d, J = 8.0 Hz; -NHTFA), 10.02 (1H, s; =NOH).

Step 2: (1'S,1S,3R)-3 (oximoethyl)-5,10-dioxo-1 (2,3,6-trideoxy-3-trifluoroacetamido-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c] pyran (BCH-2101)

Acetylation was done on the oxime from step 1 herein (33mg; 0.051 mmole) in CH_2Cl_2 (4ml) using pyridine (0.2 ml), acetic anhydride (0.1 ml) and catalytic amount of DMAP. After stirring at room temperature for 3 hours, the mixture was poured into ice, extracted with CH_2Cl_2 (3x50 ml), washed with water (15 ml), dried and evaporated. The crude product was pumped for 16 hours before using in the next step.
CAN oxidation was done on the crude acetate (40 mg) using sodium bicarbonate following the general procedure as described in other examples. It resulted in 32 mg of crude quinone. The quinone was reacted with acetoxy butadiene (100 µl) in toluene following the general procedure. On purification through a column of silica gel (30% EtOAc in toluene, 50% EtOAc in toluene and CH_2Cl_2: MeOH=9:1 as eluents) pure tricyclic glycoside (29 mg) was obtained. Finally, deprotection of acetate and PNB groups was done by using sodium methoxide (catalytic) in methanol (3 ml) at 0°C. After stirring at 0°C for 14 minutes, the mixture was neutralized with dil. HCl to pH-7, diluted with water (5ml), extracted with CH_2Cl_2 (3x30 ml), washed with water (10 ml), dried and evaporated. The crude product was purified by column chromatography over a small column of silica gel (1% methanol in CH_2Cl_2 as eluent) and preparative TLC (CH_2Cl_2: MeOH=9:1) yielding pure titled oxime (3.7 mg; 14% in 4 steps), m.p.=125-27°C.
NMR (acetone-d_6) δ: 1.35 (3H,d,J=6.6Hz; CH_3 of the sugar), 1.75 (1H,dd,J=4.6,13.0Hz;H-2 of the sugar), 1.95 (3H,s,CH_3 of the side-chain), 3.71 (1H, br.signal; H-4 of the sugar), 4.27 (2H,m;sugar-H), 4.57 (1H,q,J=6.6Hz;H-5 of the sugar), 4.70 (1H,t,J=7.5Hz;H-3), 5.44

(1H,d,J=3.3Hz;H-1 of the sugar), 6.07 (1H,S;H-1), 7.87-7.90 (2H,m;Ar-H), 8.08-8.12 (2H,m;Ar-H), 10.15 (1H,bit br. singlet;=NOH).

Step 3: (1R,3S)-3-(oximoethyl)-1 (2,3,6-trideoxy-3-trifluoroacetamido-4-p-nitrobenzoyl-L-lyxohexopyranose)-5,8-dimethoxy-isochroman

Oxime was prepared from 3-acetyl isochroman glycoside (60 mg; .096 mmol) using hydroxylamine hydrochloride (39 mg; 0.56 mmole) in EtOH (2.6 ml) and water (0.26 ml), and sodium hydroxide (21.5 mg) in EtOH (1.3 ml) following the procedure described in step 1 herein. After chromatography over silica gel prewashed with triethylamine titled oxime (in diastereomeric mixture of 5:1 ratio) was obtained in 81% yield (50 mg).

NMR (acetone-d_6; δ): 1.10 (3H, d, J = 6.6 Hz; CH_3 of sugar), 1.98 (3H, s; methyl of the side-chain), 2.39 (1H, dt, J = 3.6, 12.9 Hz; H-4), 3.81 (6H, s; Ar-OCH_3), 4.63-4.73 (1H, m; H-3 of sugar), 5.45 (1H, br signal; H-1 of sugar; same of the other diastereomer overlapped), 5.56 (1H, br signal; H-4 of the sugar; same of the other diastereomer overlapped), 5.95 (1H, s, H-1), 6.81-6.95 (m; Ar-H), 8.30-8.43 (m; A-H of PNB group), 8.66 (1H, br d, J = 5.9 Hz; NHTFA), 10.05 (1H, s; =N-OH), (There were few other signals which were due to the other diastereomer and to a small impurity which were not detailed.).

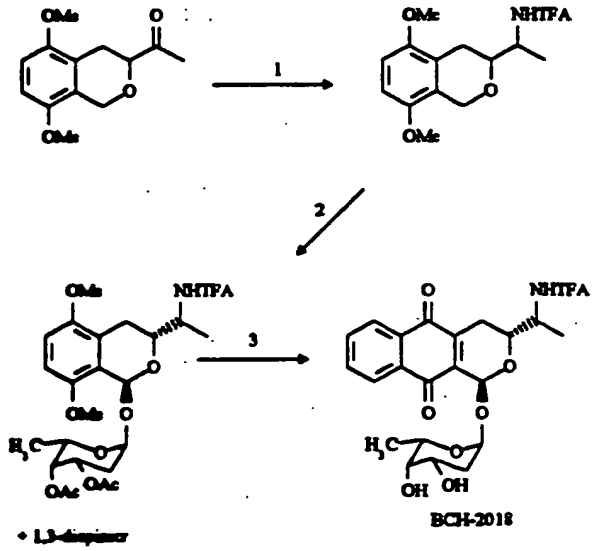
Step 4: (1'S, 1R, 3S)-3 (oximoethyl)-5,10-dioxo-1 (2,3,6-trideoxy-3-trifluoroacetamido-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-(2,3-c)-pyran (BCH-2115)

Acetylation of the oxime (50 mg; .078 mmole) was done following the procedure described in step 2, first part. CAN oxidation was done on the acetate (54 mg) using sodium bicarbonate following the general procedure. It resulted in 50 mg of crude quinone. Quinone (50 mg) was reacted with acetoxybutadiene (0.1 ml) in toluene (2 ml) following the general procedure. On purification by column chromatography over silica gel (20% EtOAc in toluene, 50% EtOAc in toluene and 5% methanol in CH_2Cl_2 as eluents) gave 33 mg of slightly impure tricyclic compound. Finally, deprotection of acetate and PNB groups was done by using sodium methoxide (catalytic) in methanol (2 ml) at 0°C following the procedure described in step 2, last part. The titled crude product was passed

through two columns of silica gel (1% and 2% methanol in CH_2Cl_2 as eluents) yielding the oxime in 12.5% yield (5 mg) (contaminated with the other diastereomer in 5.6:1 ratio).

NMR (acetone-d_6; δ): 1.18 (3H,d,J=6.4Hz;CH_3 of the sugar), 1.76 (1H,dd,J=4.8,12.9Hz;H-2 of the sugar), 1.98 (3H,s,CH_3 of the side chain), 2.18 (1H, dd,J=3.7,12.9Hz,H-4), 3.67 (1H,br.d,J=3.9Hz;sugar-H), 4.21-4.29 (2H,m,sugar-H), 4.77 (1H,dd,J=5.4, 9.6Hz;H-3), 5.48 (1H,d,J=3.2; H-1 of the sugar), 5.91 (1H,s,H-1), 7.86-7.92 (2H,m;Ar-H), 8.06-8.10 (2H,m;Ar-H), 10.14 (1H,s,=N-OH) , (there were small signals due to the other diastereomer present in the spectrum which were not detailed).

Example 42: **Preparation of (1'S,1S,3R)-3 (trifluoroacetamidoethyl)-5,10-dioxo-1 (2,3,6-trideoxy-3,4-dihydroxy-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho [2,3-c] pyran (BCH-2018)**



Step 1: **3-(Trifluoroacetamido-ethyl)-5,8-dimethoxy isochroman**

To a solution of hydroxylamine-hydrochloride (1.4 g; 20.1 mmole) in a mixture of ethanol (30 ml) and water (3 ml) was added sodium hydroxide (720 mg) in ethanol (15 ml). The mixture was stirred for .5 hour. The solution was filtered. The filtrate was added to 5,8-dimethoxy-3-acetyl-isochroman (1 g; 4.23 mmole). The mixture was stirred at room temperature for 1.5 hour and evaporated to dryness. The residue was

dissolved in small volume of water (10 ml), extracted with CH_2Cl_2 (3x100 ml), washed with brine (20 ml), dried and evaporated. The crude product (900 mg) obtained was dissolved in toluene (30 ml) and cooled to -40°C. Red-Al (9 ml) was added during 25 minutes. The mixture was stirred at -40°C for 40 minutes. The temperature of the cooling mixture was raised slowly to 25°C and the reaction was stirred at 25°C for 16 hours. Excess reagent was destroyed by careful addition of cold water (6 ml) followed by 10% sodium hydroxide (1 ml). The mixture was extracted with ether (3x100 ml), washed with brine (25 ml), dried and evaporated. The crude product (800 mg) was dissolved in CH_2Cl_2 (50 ml). Pyridine (8 ml) and DMAP (15 mg) were added and the mixture was cooled to 0°C. Trifluoroacetic anhydride (3 ml) was added slowly and the mixture was stirred at room temperature for 16 hours. It was poured into ice, neutralized with saturated sodium bicarbonate, extracted with CH_2Cl_2 (3x100 ml), washed with water (25 ml), dried and evaporated. The solid residue was recrystallized twice from a mixture of hexane and ether (4:1) yielding pure titled product (purity by NMR: >92%; yield = 330 mg; 23.4% in three steps).

NMR ($CDCl_3$; δ): 1.29 (3H, d, J = 6.8 Hz; $-CH_3$), 2.52 (1H, dd, J = 11.3, 16.9 Hz; H-4), 2.69 (1H, dd, J = 2.2, 16.4 Hz; H'-4), 3.65 (1H, ddd, J = 3.2, 6.3, 11.2 Hz; H-3), 3.75, 3.78 (3H, s each, Ar-OCH_3), 4.24 (1H, m; $-CH(NHCOCF_3)CH_3$), 4.58 (1H, d, J = 15.8 Hz; H-1), 4.97 (1H, d, J = 15.8 Hz; H'-1), 6.62, 6.67 (1H, d each, J = 8.9 Hz; Ar-H).

Step 2: (1S',1S,3R)-3-(trifluoroacetamidoethyl)-5,8-dimethoxy-1-(2',3',6'-trideoxy-3',4'-dihydroxy-L-lyxohexopyranose)-isochroman

Coupling with sugar was done using DDQ in CH_2Cl_2 following general procedure (step 1, example 14). The product was isolated as diastereomeric mixture from crude reaction mixture by column chromatography over silica gel prewashed with .5% triethylamine (eluent:hexane:ethyl acetate = 80:20) in 75% yield.

To a solution of the diastereomeric mixture (100 mg) in CH_3CN (6 ml) at 0°C was added 0.1 N NaOH (4 equiv.). The mixture was stirred at 0°C for .5 hour. Ice bath was removed and it was stirred at room temperature for 1.5hr. The mixture was diluted with water (10 ml), extracted with CH_2Cl_2 (3x100 ml), washed with water (20 ml), dried and evaporated. The crude product was chromatographed over silica gel

(prewashed with .2% triethylamine) eluent: 50%, 60%, 70%, 80% EtOAc in hexane and finally by pure EtOAc) yielding pure title compound (yield = 25 mg; 29.4%), and 1,3-diepimer (37 mg; 80% pure; 34.5%).

NMR (Acetone-d_6;δ) of the title compound: 1.28, 1.35 (3H,d each, J = 6.5 Hz; CH_3 of the side chain and CH_3 of the sugar), 1.58 (1H, dd, J = 5.1,12.6 Hz; H-2 of the sugar), 1.91 (1H, dt, J = 3.8, 12.3 Hz; H-2 of the sugar), 2.41 (1H, dd, J = 11.6, 17.4 Hz, H-4), 2.79 (1H, dd, J = 3.4, 17.6 Hz; H'-4), 3.42 (1H, d, J = 4.4, sugar-H), 3.55 (1H, br signal; H-4 of the sugar), 3.64 (1H, d, J = 6.7 Hz; sugar-H), 3.77, 3.78 (3H, s, each, Ar-OCH_3), 4.16-4.29 (2H, m, -CH(NHTFA)CH_3 and sugar-H), 4.36 (1H, q, J = 6.5 Hz; H-5 of sugar), 5.36 (1H, d, J = 3.3 Hz; H-1 of the sugar), 6.04 (1H, s, H-1), 6.79, 6.88 (1H, d each, J = 8.9Hz; Ar-H), 8.50 (1H, br d, J = 7.0; NHTFA).

NMR of 1,3-diepimer (acetone-d_6; δ): 1.21 (3H, d, J = 6.5 Hz; CH_3), 1.36 (3H, d, J = 6.3 Hz; CH_3), 2.37 (1H, dd, J = 6.1, 11.3 Hz; H-4), 2.80 (1H, dd, J = 3.3, 17.3 Hz; H'-4), 3.45 (1H, d, J = 4.8 Hz; sugar-H), 3.53 (1H, br signal; sugar-H), 3.66 (1H, d, J = 6.9 Hz; sugar-H), 3.78, 3.81 (3H, s each; Ar-OCH_3), 4.08 (1H, q, J = 6.7 Hz; H-5 of the sugar), 4.16-4.29 (2H, m; CH(NHTFA)CH_3 and sugar-H), 5.36 (1H, br singlet, H-1 of sugar), 5.85 (1H, s; H-1), 6.78-6.89 (2H, m; A-H), (There were few signals due to the other diastereomer which are not detailed.).

Step 3: (1'S,1S,3R)-3-(trifluoroacetamidoethyl)-5,10-dioxo-1-(2',3',6'-trideoxy-3',4'-dihydroxy-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran (BCH-2018)

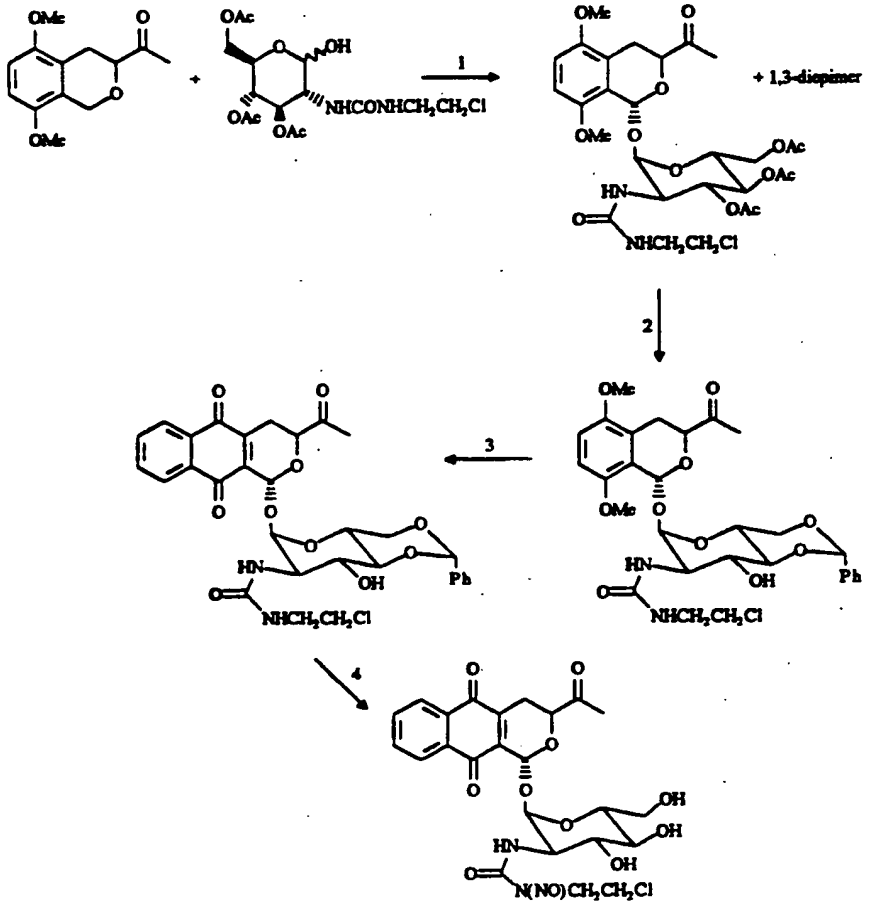
CAN oxidation was done on dimethoxy-compound following the general procedure (step 3, example 12).

The crude quinone was reacted with acetoxy-butadiene in toluene following the general procedure. Pure titled product was obtained by column chromatography over silica gel (eluent: toluene: EtOAc=70:30 and 60:40) followed by preparative TLC (eluent: CH_2Cl_2: MeOH=9:1) (5 mg;19% yield) as a light yellow solid, mp: 180-3°C (dec.).

NMR (acetone-d_6;δ): 1.34 (3H,d,J=6.4Hz;-CH_3), 1.38 (3H,d,J=6.7Hz;-CH_3), 1.60 (1H,dd,J=4.7,12.6Hz;H-2 of the sugar), 1.92 (1H,dd,J=3.7,12.2Hz;H-2 of the sugar), 2.47 (1H,dd,J=10.2,19.0Hz;H-4), 2.82 (1H,dd,J=2.9,19.0Hz;H'-4), 3.49 (1H,d,J=4.3Hz;-OH of the sugar), 3.59 (1H,br.signal which became sharp on D_2O-exchange;H-4 of sugar), 3.68

(1H,d,J=6.7Hz;-OH of the sugar), 3.82 (1H,m;H-3), 4.19-4.30 (2H,m,overlapping-CHCH$_3$(NHTFA) and sugar-proton), 4.42 (1H,q,J=6.5Hz,H-5 of the sugar), 5.36 (1H,d,J=3.5Hz,H-1 of the sugar), 6.0 (1H,s,H-1), 7.86-7.90 (2H,m;Ar-H), 8.05-8.10 (2H,m;Ar-H), 8.56 (1H,br. signal;-NHTFA). (Stereochemistry of NHTFA is not yet determined).

Example 43: **Preparation of (1'R,1R,3S)-3-aceto-5,10-dioxo-1-(2-deoxy-2-chloroethylnitrosoureido-D-glucopyranose)-3,4,5,10-tetrahydro-1H-naphtho [2,3-c] pyran (BCH-2038)**



BCH-2038

Step 1: **(1'R, 1R, 3S)-3-aceto-5,8-dimethoxy-1(2-deoxy-2-chloroethylureido-3,4,6-triacetyl-D-glucopyranose)-isochroman.**

2-Deoxy-2-chloroethylureido-3,4,6-triacetyl-D-glucopyranose was prepared following known procedure (Ref: T.P. Johnston, G.S. McCaleb and J.A. Montgomery, J. Med. Chem., 18, 104 (1975)). This compound was coupled with 3-aceto-5,8-dimethoxy-isochroman using DDQ following the general procedure outlined before (step 1, example 14). Purification was done by column chromatography over silica gel (eluent:hexane:EtOAc = 7:3) yielding the title compound (29.4%) and 1,3-diepimer (31%).

NMR (acetone-d_6; δ) of the title compound: 1.91, 1.95, 2.00 (3H, s each; acetyl groups) 2.32 (3H, s, keto-methyl), 2.50 (1H, dd, J = 12.3, 17.6 Hz; H-4), 3.01 (1H, dd, J = 4.0, 17.6 Hz; H'-4), 3.49 (2H, m; -NH-CH_2- group), 3.63 (2H, t, J = 6.2 Hz; -CH_2-Cl group); 3.83, 3.88 (3H, s each; Ar-OCH_3), 4.14 (4H, m; H-5, H-2, H-6 and H-6 of the sugar overlapping), 4.60 (1H, dd, J = 4.1, 12.2 Hz; H-3), 5.08 (pair of double-doublets overlapping; H-3 and H-4 of the sugar), 5.46 (1H, d, J = 3.5 Hz; H-1 of the sugar), 5.49 (1H, broad s; -NH-CO-), 6.02 (1H, s; H-1), 6.15 (1H, br signal; CONH-CH_2), 6.87, 6.96 (1H, d each, J = 9.0 Hz; Ar-H).

NMR (acetone-d_6; δ) of the 1,3-diepimer: 1.92, 2.00, 2.06 (3H, s each; acetate-groups), 2.28 (3H, s; keto-methyl), 2.48 (1H, dd, J = 12.0, 17.8 Hz; H-4), 2.91 (1H, dd, J = 4.2, 11.7 Hz; H'-4), 3.26-3.51 (2 multiplets, 1H each; -HN-CH_2-), 3.56 (2H, t, J = 6.2 Hz; -CH_2Cl), 3.84 (6H, s; Ar-OCH_3), 4.14-4.23 (2H, m; sugar-H), 4.34 (1H, dd, J = 4.7; 12.1 Hz; sugar-H), 4.62 (2H, dd, another proton overlapped; J = 4.3, 12 Hz; H-3), 5.05-5.18 (2H, m; H-3 and H-4 of sugar), 5.51 (1H, d, J = 3.7 Hz; H-1 of the sugar), 5.81 (1H, d, J = 9.6 Hz; -NH-CO), 5.98 (1H, br, triplet; -NH-CH_2), 6.16 (1H, s; H-1), 6.91, 6.99 (1H, d each, J = 9.0 Hz; Ar-H).

Step 2: (1'R, 1R, 3S)-3-aceto-5,8-dimethoxy-1(2-deoxy-2-chloroethylureido-4,6-benzylidene-D-glucopyranose)-isochroman

To a cold solution of triacetyl derivative (120 mg; .19 mmol) in CH_3CN was added .1 N NaOH (8.6 ml; 4.6 eq.). The mixture was stirred at 0°C until TLC revealed complete reaction. It was carefully neutralized with .1 N HCl to pH ~8 and extracted with ethyl acetate (3x100 ml), washed with 2.5% $NaHCO_3$-NaCl-solution (1:1) (10 ml), dried and evaporated. To a solution of the crude product in DMF (5 ml), benzaldehyde dimethyl acetal (30 µl; 1.2 eq.) and p-TSA (10 mg; catalytic) was added. The

reaction flask was connected to water aspirator and held at 50°C for 15 minutes. Sodium bicarbonate solution (2.5%; 10 ml) was added and the mixture was extracted with CH_2Cl_2 (3x50 ml), washed with saturated NaCl solution, dried and evaporated. The crude product was washed with a mixture of hexane and ether, yielding pure titled benzylidene derivative (77 mg; 68%).

NMR (acetone-d_6; δ): 2.33 (3H, s, keto-methyl), 2.50 (1H, dd, J = 12.2, 17.6 Hz; H-4), 2.99 (1H, dd, J = 4.1, 17.6 Hz; H'-4), 3.49 (2H, t, J = 5.8 Hz; $-CH_2-Cl$), 3.63 (2H, m, $-NH-CH_2-$), 3.82, 3.91 (3H, s, Ar-OCH_3), 4.19 (1H, dd, J = 4.5, 9.6 Hz; sugar-H), 4.62 (1H, dd, J = 4.1, 12.2 Hz; H-3), 5.46 (1H, d, J = 3.8 Hz; H-1 of the sugar), 5.62 (1H, s, -CH Ph), 5.68 (1H, d, J = 8.5 Hz; -NH-), 6.00 (1H, s, H-1), 6.18 (1H, br s, -NH CH_2-), 6.87, 6.95 (1H, d each, J = 8.9 Hz; Ar-H), 7.34 (3H, m; Ar-H), 7.46 (2H, m; Ar-H).

Step 3 **(1'R, 1R, 3S)-3-aceto-5,10-dioxo-1-(2-deoxy-2-chloroethylureido-4,6-benzylidene-D-glucopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-C] pyran**

To a solution of benzylidene derivative (77 mg; .127 mmol) in acetonitrile (6 ml) was added a solution of ceric ammonium nitrate (146 mg; .266 mmol) in water (2.5 ml) at room temperature. The mixture was stirred for 5 minutes, diluted with water (10 ml), extracted with CH_2Cl_2 (3x75ml), washed with water (15 ml), dried, evaporated. The crude product (60 mg) was pumped for 2 hours before going to the next step. The crude product was taken up in dry toluene (3 ml) and acetoxy-butadiene (1.2 ml) was added. The mixture was stirred at room temperature for 16 hours. The solution was not quite homogeneous and TLC showed some starting material. Acetoxy-butadiene (.5 ml) was further added and stirred for 20 hours. The mixture was diluted with toluene (10 ml). Silica gel (500 mg) was added and air was bubbled through the mixture for 1 hour. The crude reaction mixture was passed through a column of silica gel (eluent:toluene:EtOAc = 7:3 and CH_2Cl_2:MeOH = 9:1). Fraction containing the product was further purified by preparative TLC (eluent:EtOAc) yielding 12 mg of pure titled product (15%) (poor yield because of separation problem).

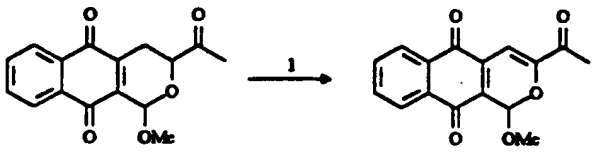
NMR (acetone-d_6; δ): 2.35 (3H, s; keto-methyl), 2.58 (1H, dd, J = 11.4, 19.7 Hz; H-4), 3.01 (1H, dd, J = 3.9, 19.6 Hz; H'-4) 3.55, 3.67 (m each, HN CH_2-CH_2Cl), 4.22 (1H, dd, J = 4.6, 9.7 Hz; sugar-H), 4.65 (1H, d, J =

3.9 Hz; -OH), 4.73 (1H, dd, J = 4.0, 11.4 Hz; H-3), 5.52 (1H, d, J = 3.8 Hz; H-1 of the sugar), 5.63 (2H, br s; CH-Ph and -NH-CO), 5.94 (1H, t, J = 5.7 Hz; $-NH-CH_2$), 6.04 (1H, s; H-1), 7.33 (3H, m, Ar-H), 7.46 (3H, m; Ar-H), 7.91 (2H, m, Ar-H), 8.14 (2H, m; Ar-H).

Step 4: **(1'R, 1R, 3S)-3-aceto-5,10-dioxo-1-(2-deoxy-2-chloroethyl-nitrosoureido-D-glucopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-C] pyran**

To a solution of benzylidene derivative (6 mg; .01 mmol) in 96% formic acid (1 ml) at 5°C was added $NaNO_2$ (10 mg) in two portions. The reaction was complete in 2 minutes. It was diluted with water (5 ml), extracted with CH_2Cl_2 (3x25 ml), washed with water (10 ml; 15 ml), dried over Na_2SO_4 and evaporated. The crude product (4.5 mg) was passed through a small column of silica gel (eluent:EtOAc and 10% methanol in CH_2Cl_2) yielding pure titled product (yield = .9 mg; 17%) (HPLC:92%) NMR (acetone-d_6; δ): 2.35 (3H, s, keto-methyl), 2.51 (1H, dd, J = 12.9, 19.2 Hz; H-4), 2.98 (1H, dd, J = 4.1, 19.6 Hz; H'-4), 3.52-3.89 (two multiplets; some of the sugar protons, and overlapping A_2B_2 system due to $-HN(CH_2)_2Cl$), 4.08 (H, dd, J = 3.5, 6.0 Hz; sugar-H), 4.26 (1H, dd, J = 6.6, 11.3 Hz; sugar-H), 4.43 (1H, dd, J = 4.7, 7.5 Hz; sugar-H), 4.66 (1H, dd, J = 4.0, 11.5 Hz; H-3), 5.66 (1H, d, J = 3.6; H-1 of the sugar), 5.99 (1H, s, H-1), 7.59 (1H, d, J = 8.6 Hz; NH-CO), 7.88, 8.08 (two multiplets, Ar-H).

Example 44: **Preparation of 3-aceto-5,10-dioxo-1-methoxy-5,10-dihydro-1H-naphtho [2,3-c] pyran (BCH-2129)**



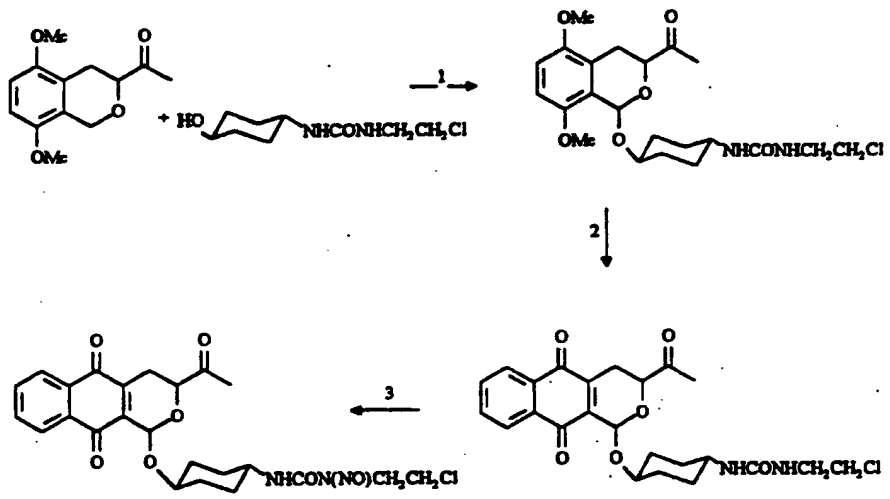
BCH-2129

Step 1: **3-Aceto-5,10-dioxo-1-methoxy-5,10-dihydro-1H-naphtho-(2,3-c)-pyran (BCH-2129)**

To a solution of 3-acetyl-5,10-dioxo-1-methoxy-3,4-5,10-tetrahydro-1H-naphtho (2,3-c) pyran (50 mg, .175 mmole) in CH_3CN (8 ml) and THF (4 ml)

at 0°C was added 0.5N sodium hydroxide (1 equiv.). The mixture was stirred at 0°C for 15 minutes and it was allowed to come to room temperature. After 1.5 hour at room temperature the mixture was acidified with dil. HCl to pH-6. Saturated NH_4Cl (5 ml) was added and the mixture was extracted with CH_2Cl_2 (3x50 ml), washed with water (10 ml), dried and evaporated. The crude titled product was subjected to preparative TLC (eluent: toluene:EtOAc=96:4) and pure product was isolated as a light yellow solid, mp. 154-56°C (3mg; 6%).
NMR (acetone-d_6, δ): 2.50 (3H,s,ketomethyl), 3.63 (3H,s,-OCH_3), 6.42 (1H,s,H-1), 7.11 (1H,s;H-4), 7.92 (2H,m;Ar-H), 8.14 (2H,m;Ar-H).

Example 45: **Preparation of (1R,3S) and (1S,3R)-3-aceto-5,10-dioxo-1 (4-chloroethylnitrosoureido cyclohexyl-oxy)-3,4,5,10-tetrahydro-1H-naphtho [2,3-c] pyran (BCH-2114)**



BCH-2114

Step 1: **(1R,3S) and (1S,3R)-3-Aceto-1 (4-chloroethylureido-cyclohexyloxy)-5,8-dimethoxy-isochroman**

3-Acetyl isochroman was coupled to 4-chloroethyl ureido-cyclohexanol (prepared by known procedure, ref.: T.P. Johnston, G.S. McCaleb, P.S. Opliger, W.R. Laster and J.A. Montgomery, J. Med. Chem., 14, 600 (1971)) using DDQ following the general procedure (step 1, example 14). Enantiomeric mixture of the titled products was isolated from the crude

reaction mixture by column chromatography over silica gel (eluent: 50% and 80% EtOAc in hexane) yield=100mg (52%).

NMR (acetone-d_6;δ): 1.26-1.48 (two multiplets; CH_2-groups of cyclohexyl ring), 1.78-1.80 (multiplet,-CH_2 of cyclohexyl ring), 2.27 (3H, s, keto-methyl), 2.45 (1H, dd, J = 12.1, 17.8 Hz; H-4), 2.90 (1H, dd, J = 4.2, 17.7 Hz; H'-4), 3.42 (2H, m; -HNCH_2Cl), 3.59 (2H, t, J = 6.0 Hz; -CH2-Cl), 3.78, 3.79 (3H, s each, Ar-OCH_3), 3.86 (1H, m; H-1 of the cyclohexyl ring), 4.61 (1H, dd, J = 4.2, 12.0 Hz; H-3), 5.51 (1H, d, J = 7.4 Hz; -NH-CO-), 5.67 (1H, br signal; -CONHCH_2-), 5.90 (1H, s, H-1), 6.79, 6.87 (1H, d each, J = 8.9 Hz; Ar-H).

Step 2: (1R,3S) and (1S,3R)-3-Aceto-5,10-dioxo-1 (4-chloroethylureido cyclohexyl-oxy)-3,4,5,10-tetrahydro-1H-naphtho-(2,3-c)-pyran

CAN oxidation was performed on the dimethoxy-isochroman from step 1 herein (35 mg; .077 mmole) following the general procedure (step 2, example 14).

The crude product (32 mg) was dissolved in dry toluene (3 ml) and acetoxybutadiene (0.5 ml) was added. The mixture was stirred at room temperature for 18 hours. Silica gel (500 mg) was added and air was bubbled for .5 hour. The crude product was passed through a column of silica gel (30% EtOAc in toluene, 50% EtOAc in Toluene, and CH_2Cl_2: MeOH=19:1 as eluents) yielding pure tricyclic titled compounds (15 mg; yield 41%).

NMR (acetone-d_6;δ): 1.24-1.54 (6H, m, CH_2 group of the cyclohexyl ring), 2.30 (3H, s, ketomethyl), 2.51 (1H, dd, J = 11.6, 19.5 Hz; H-4), 3.42 (2H, m; -NHCH_2-CH_2Cl), 3.60 (2H, t, J = 6.2 Hz; -CH_2Cl), 3.95 (1H, m, H-1 of the cyclohexyl ring), 4.64 (1H, dd, J = 4.2, 11.5 Hz; H-3), 5.54 (1H, br d, J = 6.9 Hz; NHCO-), 5.69 (1H, br signal; -CONH-CH_2-), 5.92 (1H, s; H-1), 7.86-7.91 (2H, m; Ar-H), 8.06-8.10 (2H, m; ArH).

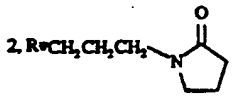
Step 3: (1R,3S) and (1S,3R)-3-aceto-5,10-dioxo-1 (4-chloroethylnitrosoureido cyclohexyl-oxy)-3,4,5,10-tetrahydro-1H-naphtho-(2,3-c)-pyran (BCH-2114)

To a solution of chloroethyl ureido-derivative from step 2 herein (14 mg, .03 mmole) in formic acid (1.2 ml) at 5°C was added sodium nitrite (20 mg) in two portions. Reaction was complete in 3 minutes. It was

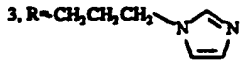
diluted with water (10 ml), extracted with CH_2Cl_2 (3x50 ml), washed with water (2x10 ml), dried and evaporated. The crude product was purified by passing through a small column of silica gel (eluent: 1% methanol in CH_2Cl_2) and finally by washing with hexane-ether mixture yielding pure titled nitroso-derivative, mp=58-63°C (yield=5 mg;34%).
NMR (acetone-d_6;δ): 1.48-1.80 (6H,m;CH_2 of the cyclohexyl group), 2.32 (3H,s,ketomethyl), 2.52 (1H,dd,J=11.6, 19.6Hz;H-4), 2.93 (1H,dd,J=4.3,19.7Hz;H'-4), 3.60 (2H,t,J=6.5Hz;-CH_2-Cl), 3.76-4.05 (m,H-1 and H-4 of the cyclohexyl group), 4.16 (2H,t,J=6.6Hz;-N(NO)CH_2-), 4.66 (1H,dd,J=4.3,11.4Hz;H-3), 5.97 (1H,s,H-1), 7.77 (1H,br.d, J=7.8Hz;-NHCO-), 7.87-7.90 (2H,m;Ar-H), 8.07-8.11 (2H,m;Ar-H).

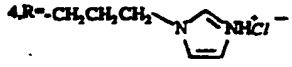
Example 46: Using the same carboxylic acid as described in Example 16, 1-methoxy-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran-3-carboxamides were prepared

Step: 1, R=-C6H5 BCH-2044



BCH-2166





BCH-2157

Step 1: 1-methoxy-3-N-anilinylcarbonyl-5,10-dioxo-5,10-dihydro-1H-naphtho-[2,3-c]-pyran (BCH-2044)

Using a similar procedure as described in step 7, example 16, the carboxylic acid from step 6, example 16, was converted to the titled compound.
dec. 140°C; m.p. 200°C.

^{1}H NMR ($CDCl_3$, 250 MHz, Bruker): δ, 3.68 (3H, s, OCH_3), 6.48 (1H, s, 1-CH), 7.18 (1H, tr, J = 7.6 Hz, p-Ani-H), 7.49 (2H, tr, J = 8.0 Hz, m-Ani-H), 7.50 (1H, s, 4-CH), 7.66 (2H, d, J = 7.8 Hz, O-Ani-H), 7.79 (2H, m, 7, 8-ArH), 8.15 (2H, m, 6, 9-ArH), 8.40 (1H, s, NHCO).

IR (Nicolet , 205 FT, film on NaCl plate): cm^{-1}, 3322.9, 2929.3 2848.3, 1682.9, 1659.8, 1594.2, 1527.7, 1443.7, 1374.2, 1297.0, 1258.4, 1063.2, 947.6, 863.1, 719.7, 693.6.

Step 2: 1-methoxy-3-(3-N-pyrrolidinonylpropylaminocarbonyl)-5,10-dioxo-5,10-dihydro-1H-naphtho-[2,3-c]-pyran (BCH-2166)

60 mg of the acid from step 6, example 16, was dissolved in 6.8 ml of dry THF, cooled to 0°C and 63 µl of oxalyl chloride was added. The mixture was allowed to stir at 0°C for 20 minutes, and then at room temperature for 20 minutes. The solvent was then evaporated, the residue was redissolved in dichloromethane and evaporated, and then the residue was again dissolved into dry THF. The solution was cooled to -10°C. 29.3 µl of triethylamine and 19.90 µl of 1-(3-aminopropyl)-2-pyrrolidinone was added and allowed to stir for 45 minutes at -10°C and then 2 hours at room temperature. The solvent was then evaporated to half of its original volume, the remaining solution was poured onto sat. brine and extracted into dichloromethane. The organic layer was then washed with sat. sodium bicarbonate solution, dried over sodium sulfate, and evaporated to dryness to give 24 mg of pure titled product.

NMR ($CDCl_3$ 250 MHz, Bruker): δ, 1.86 (2H, Quin, J = 6.6 Hz, C-CH_2-C), 2.08 (2H, Quin, J = 7.5 Hz, 4'-pyrr-CH_2), 2.45 (2H, t, J = 7.5 Hz, 3'-pyrr-CH_2), 3.15-3.34 (2H, m, CONHCH_2), 3.36-3.55 (4H, m, CH_2-pyrr, 5'-pyrr-CH_2), 3.74 (3H, s, -OCH_3), 6.43 (s, 1H, 4-CH), 7.32 (s, 1H, 1-CH), 7.70-7.78 (2H, m, 6, 9-ArH), 8.08-8.16 (3H, m, 7, 8-ArH, NH).

IR (Nicolet, 205 FT, film on NaCl plate): cm^{-1}, 3320.9, 2936.7, 2871.3, 1679.9, 1658.1, 1597.0, 1527.2, 1335.2, 1291.5, 1278.4, 1082.1, 947.98, 857.41, 801.34, 723.70.

Step 3: (3-N-imidazolylpropyl)-1-methoxy-5,10-dioxo-5,10-dihydro-1H-naphtho-[2,3-c]-pyran-3-carboxamide

To a stirred solution of acod from step 6, example 16, (0.185 mmol, 53 mg) and catalytic amounts of DMF in 6 ml of THF at 0°C was added oxalyl chloride (0.426 mmol). After stirring at 0°C for one hour, and at room

temperature for a further 20 minutes, the solvent was evaporated to dryness. 6 ml of THF was then added, and the mixture divided into two. 3 ml of solution was then cooled to -10°C, and 1-(3-amminopropyl)-imidazole (8.39 µl, 0.20 mmol) dissolved in 1 ml of THF was added dropwise. The mixture was allowed to stir for one hour at which time it was poured onto sat. sodium bicarbonate solution, extracted into methylene chloride, washed with brine, dried over sodium sulfate and the solvent evaporated. Purification on TLC using 8% methanol/chloroform system produced 6 mg of pure titled product.

^{1}H NMR (acetone -d_6, 250 MHz, Bruker), δ: 2.10 (m, 2H, CH_2-imidazol), 3.42 (m, 2H, C-CH_2-C), 3.60 (s, 3H, OCH_3), 4.14 (t, 2H, CH_2NCO, 6.34 (s, 1H, 4-CH), 6.96 (s, 1H, 4-CH (imidazol)), 7.16 (s, 1H, 1-CH), 7.18 (s, 1H, 5-CH (imidazol)), 7.70 (s, 1H, 2-CH (imidazol)), 7.90 (m, 2H, 6, 9-ArH), 8.12 (m, 2H, 7, 8-ArH), 8.29 (m, 1H, NH).

IR (Nicolet 205 FT, film on NaCl plate), cm^{-1}: 3313.5, 2932.1, 2853.4, 1676.1, 1665.4, 1593.2, 1552.8, 1334.1, 1274.0, 1087.5, 950.72, 859.52, 718.64.

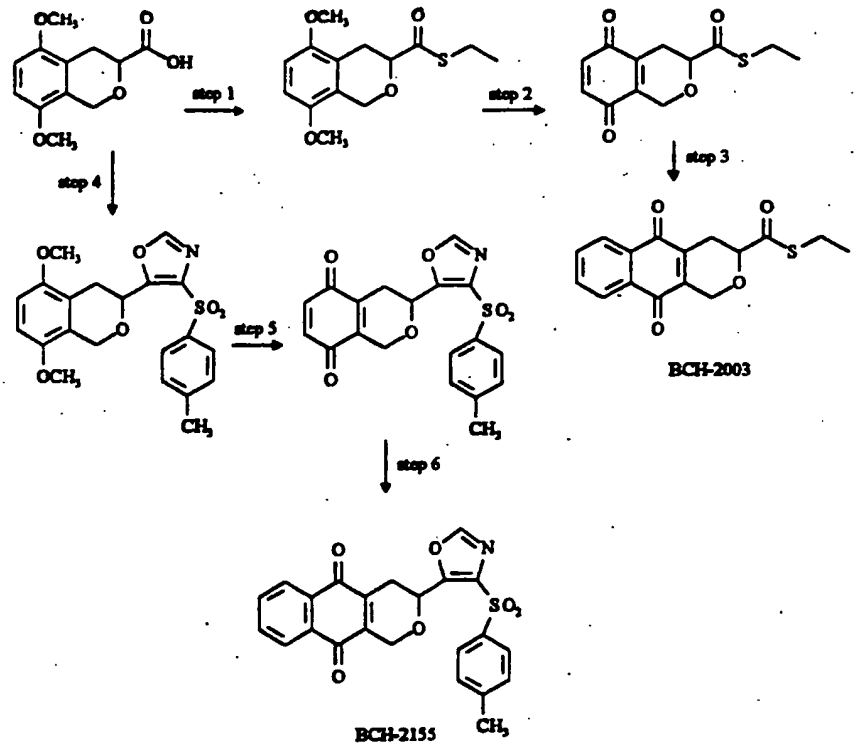
Step 4: (3-N-hydrochloroimidazolylpropyl)-1-methoxy-5,10-dioxo-5,10-dihydro-1H-naphtho-[2,3-c]-pyran-3-carboxamide (BCH-2157)

6 mg of product from step 3 herein was dissolved in 2 ml of ether. To this was added 6 µl of 1M HCl/ether solution (from Aldrich). The mixture was stirred, and then the solvent evaporated to give 6.7 mg of the HCl salt.

^{1}H NMR (acetone-d_6, 250 MHz, Bruker) for salt, δ: 2.29 (m, 2H, CH_2-imidazol), 3.53 (m, 2H, C-CH_2-C), 3.62 (s, 3H, OCH_3), 4.50 (m, 2H, CH_2NHCO), 6.33 (s, 1H, 4-CH), 7.14 (s, 1H, 1-CH), 7.55 (s, 1H, 5-CH(imi)), 7.76 (s, 1H, 4-CH(imi)), 7.88 (m, 2H, 7, 8-ArH), 8.05 (m, 2H, 6, 9-ArH), 8.64 (m, 1H, NH), 9.285 (s, 1H, 2-CH(imi)).

IR (Nicolet 205 FT, film on NaCl plate) cm^{-1}: 3345.8, 1676.5, 1652.2, 1527.0, 1280.4, 1090.9, 955.01.

Example 47: Preparation of 3-ethylthiocarbonyl-1,3,4,5,10-pentahydro-5,10-dioxo-naphtho-[2,3-c] pyran (BCH-2003) and 3-(5'-tosyloxazolyl)-1,3,4,5,10-pentahydro-5,10-dioxo-naphtho-[2,3-c]-pyran (BCH-2155)



Step 1: 3-ethylthiocarbonyl-5,8-dimethoxy-isochroman

5,8-dimethoxy-3-carboxyisochroman (300 mg, 1.26 mmol) in THF (6 ml) was stirred with 1,1'-carbonyldiimidazole (225 mg, 1.386 mmol) at room temperature for 30 minutes. More THF (6 ml) was added to dilute the forming suspension. After one hour, ethanethiol (103 µl, 1.40 mmol) was added and the mixture was stirred for 18 hours at room temperature. Solvent was evaporated and the crude titled product was chromatographed (hex:EtOAc = 4:1) to give desired product as a solid (200 mg, m.p. 99.2° C).

^{1}H NMR ($CDCl_3$, 250 MHz, Bruker): δ, 1.28 (3H, tr, J = 7.6 Hz, CH_3), 2.68 (1H, dd, J = 17.6 Hz, 11.2 Hz, 4-HCH_a), 2.92 (1H, qua, J = 7.6 Hz, $-CH_2-$), 3.12 (1H, dd, J = 11.2 Hz, 3.5 Hz, 4-HCH_e), 3.76 (3H, s, OCH_3), 3.78 (3H, s, OCH_3), 4.24 (1H, dd, J = 11.2 Hz, 3.0 Hz, 3-CH), 4.70 (1H, d, J = 15.3 Hz, 1-HCH_a), 5.06 (1H, d, J = 15.3 Hz, 1-HCH_e), 6.64 (1H, d, J = 8.0 Hz, ArH), 6.67 (1H, d, J = 8.0 Hz, ArH).

IR (Nicolet , 205 FT, film on NaCl plate): cm^{-1}, 2936.2 2836.2, 1679.2 1604.8, 1486.8, 1461.8, 1258.5 ,1094.3, 1078.9, 1022.5, 796.81, 714.69.

Step 2: 3-ethylthiocarbonyl-5,8-dioxo-1,3,4,5,8-penta-1H-benzo-[2,3-c]-pyran

The compound from step 1 herein (100 mg, 0.35 mmol) was dissolved in acetonitrile (6 ml), then cooled to 0°C. Sodium bicarbonate (58.8 mg, 0.7 mmol) was added. This was followed by addition of a solution of ammonium cerium nitrate (583 mg, .0063 mmol) in 2 ml of water. The reaction mixture was allowed stirred for 5 minutes at 0°C. TLC showed completion of the reaction. It was poured to water and extracted with methylene chloride. The organic layer was dried over Na_2SO_4 and evaporated to give a crude titled product (83 mg).

^1H NMR ($CDCl_3$, 250 MHz, Bruker): δ, 1.24 (3H, tr, J = 7.6 Hz, CH_3), 2.51 (1H, dd tr, J = 17.6 Hz, 9.2 Hz, 3 Hz, 4-HCH_a), 2.85 (1H, d, J = 17.6 Hz, 4-HCH_e), 2.88 (1H, qua, J = 7.6 Hz, -CH_2-), 4.18 (1H, dd, J = 9.2 Hz, 3 Hz, 3-CH), 4.47 (1H, d tr, J = 17.5 Hz, 3 Hz, 1-HCH_a), 4.81 (1H, br d, J = 17.6 Hz, 1-HCH_e), 6.71 (1H, d, J = 9.7 Hz, Quin-H), 6.76 (1H, d, J = 9.7 H, Quin-H).

IR (Nicolet , 205 FT, film on NaCl plate): cm^{-1}, 2972.6, 2929.5, 2882.4, 1678.5, 1655.5, 1599.3, 1418.9,. 1313.1, 1147.5, 1125.6, 993.09, 827.00, 766.77, 729.32, 667.58, 629.13.

Step 3: 3-ethylthiocarbonyl-5,8-dioxo-1,3,4,5,10-pentahydro-naphtho-[2,3-c]-pyran (BCH-2003)

The compound from step 2 herein (42 mg, 0.167 mmol) in toluene (6 ml) was stirred with 1-acetoxy-1,3-butadiene (119 µl, 1.0 mmol) at 60°C for 22 hours. Solvent was evaporated and the crude product was chromatographed (toluene/EtOAc = 100/15) to give desired titled product (41 mg) as a solid (m.p. 95.4-96.5°C).

^1H NMR ($CDCl_3$, 250 MHz, Bruker): δ, 1.26 (3H, tr, J = 7.6 Hz, CH_3), 2.65 (1H, dd tr, J = 19.4 Hz, 9.4 Hz, 3 Hz, 4-HCH_a), 2.91 (2H, qua, J = 7.6 Hz, CH_2), 3.04 (1H, d tr, J = 19.4 Hz, 3 Hz, 4-HCH_e), 4.25 (1H, dd, J = 9.4 Hz, 3 Hz, 3-CH), 4.61 (1H, d tr, J = 18.2 Hz, 3 Hz, 1-HCH_a), 4.97 (1H, dd, J = 18.2 Hz, 1.8 Hz, 1-HCH_e), 7.71 (2H, m, 7, 8-ArH), 8.04 (2H, m, 6, 9-ArH).

IR (Nicolet , 205 FT, film on NaCl plate): cm^{-1}, 2969.3, 2931.3, 2874.3, 1680.8, 1661.8, 1641.4, 1594.2, 1334.2, 1296.4, 1175.1, 1108.9, 1027.0, 874.2, 787.5, 694.6.

Step 4: 3-(5'-tosyloxasolyl)-5,8-dimethoxy isochroman

To 5,8-dimethoxy-3-carboxyisochroman (211 mg, 0.887 mmol) dissolved in THF (2.0 ml) cooled to 0°C was added oxalyl chloride (86.09 µl, 0.975 mmol). The mixture was stirred for 20 minutes then at room temperature for 20 minutes. The reaction mixture was evaporated to dryness to give desired acid chloride. It was redissolved in THF (4 ml) and cooled to -78°C. A solution of tosylmethyl isocyamide anion (made from the treatment of tosylmethyl isocyamide, 180 mg, 0.92 mmol, by n-butyllithium, 1.6 M in hexane, 0.61 ml, 0.975 mmol at -78°C for 10 minutes) was added to the above cold acid chloride solution. The reaction mixture was stirred for 24 hours as it warmed to room tempeture. Then, it was poured to NH_4Cl (sat.) and extracted with methylene chloride. The organic layer was dried (over Na_2SO_4) and evaporated to give a crude product which was chromatographed to give the desired titled product as a white solid 115 mg, m.p. 138-140°C.

^1H NMR ($CDCl_3$, 250 MHz, Bruker): δ, 2.41 (3H, s, tosy-CH_3), 2.99 (2H, d, J = 7.4 Hz, 4-CH_2), 3.76 (6H, s, 2xCH_3), 4.85 (1H, d, J = 17.5 Hz, 1-HCH_a), 4.03 (1H, d, J = 17.5 Hz, 1-H_eCH), 5.54 (1H, tr, J = 7.4 Hz, 3-CH), 6.67 (2H, br s, 6, 7-ArH), 7.33 (2H, d, J = 8.2 Hz, 3', 5', tosyl-H), 7.82 (1H, s, oxa-H), 7.92 (2H, J = 8.2 Hz, 2, 6-tosyl-H).

IR (Nicolet 205 FT, film on NaCl plate): cm^{-1}, 3134.2, 2951.5, 2837.5, 1595.5, 1511.7, 1485.6, 1463.6, 1437.5, 1331.7, 1261.6, 1194.3, 1149.0, 1089.9, 1072.0, 809.60, 798.61.

Step 5: 3-(5'-tosyloxasolyl)-5,8-dioxo-1,3,4,5,8-pentahydrobenzo-[2,3-c]-pyran

The compound from step 4 herein (10 mg, 0.024 mmol) was dissolved in acetonitrile (2 ml) and cooled to 0°C. A solution of ammonium cerium nitrate (39.5 mg, 0.072 mmol) in 0.5 ml of water was added dropwise. The reaction mixture was stirred at 0°C for 5 minutes, then poured to water and extracted with dichloromethane. The organic layer was washed with brine, dried and evaporated to give the titled compound as a white solid (9 mg, dec. 150°C; m.p. 177°C).

^1H NMR ($CDCl_3$, 250 MHz, Bruker): δ, 2.42 (3H, s, tosyl-CH_3), 2.82 (2H, m, 4-CH_2), 4.65 (1H, d tr, J = 17.6 Hz, 4.1 Hz, 1-HCH_a), 4.82 (1H, d tr, J = 17.6 Hz, 1.8 Hz, 1-HCH_e), 5.52 (1H, tr, J = 7.0 Hz, 3-CH), 6.75 (1H, d, J = 9.1 Hz, quin-H), 6.81 (1H, d, J = 9.1 Hz, quin-H), 7.35 (2H, d, J = 8.2 Hz, 3', 5'-tosyl-H), 7.83 (1H, s, oxa-H), 7.90 (2H, d, J = 8.2 Hz, 2', 6'-tosyl-H).

Step 6: **3-(5'-tosyloxazolyl)-5,10-dioxo-1,3,4,5,10-pentahydro-naphtho-[2,3-c]-pyran (BCH-2155)**

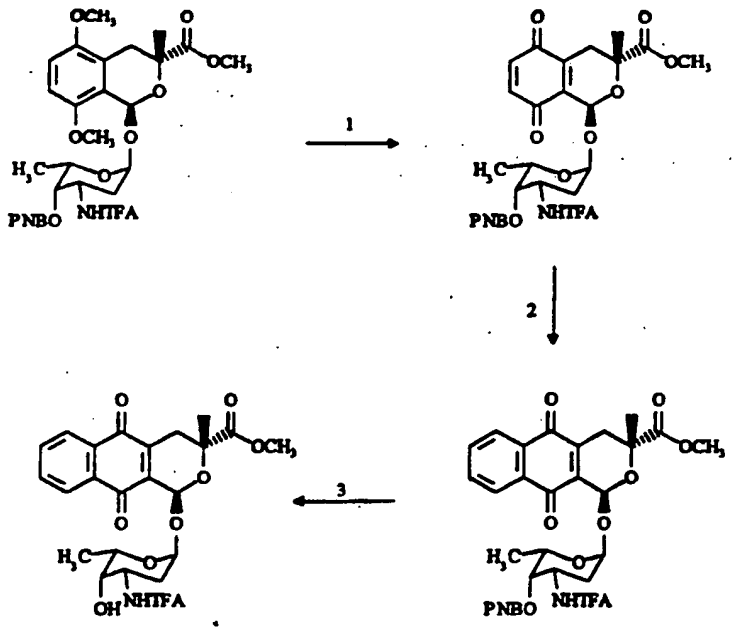
A solution of tosyloxazolyl pyranoquinone from step 5 herein in 4 ml of toluene and 0.5 ml of tetrahydrofuran (9 mg, 0.023 mmol) was heated with 1-acetoxy 1,3-butadiene (55 µl, 0.47 mmol) at 50°C for 20 hours. Solvent was evaporated to dryness and the crude product was purified by means of chromatography (Tol:EtOAc=100:15) to give desired titled product as a light colored solid (6.6 mg obtained).

M.P. >240°C.

^{1}H NMR ($CDCl_3$, 250 MHz, Bruker): δ, 2.43 (3H, s, $ArCH_3$), 2.99 (2H, m, 4-CH_2), 4.78 (1H, d tr, J = 18.8 Hz, 3.3 Hz, 1-HCH_a), 4.96 (1H, d, J = 18.8 Hz, 1-HCH_e), 5.57 (1H, dd, J = 8.9 Hz, 5.0 Hz, 3-CH), 7.36 (2H, d, J = 8.2 Hz, 3', 5'-tosyl-H), 7.75 (2H, m, 7, 8-ArH), 7.85 (1H, s, oxa-H), 7.92 (2H, d, J = 8.2 Hz, 2', 6'-tozyl-H), 8.11 (2H, m, 6, 9-ArH).

IR (Nicolet 205 FT, film on NaCl plate): cm^{-1}, 2955.7, 2921.3, 2854.0, 1662.8 (str), 1592.2, 1508.6, 1398.6, 1334.6, 1319.9, 1298. 5, 1147.6, 1106.6, 1086.9, 1013.0, 811.2, 794.8.

Example 48: **Preparation of (1'S,1S,3R)-1-(3'-trifluoroacetamido-2',3',6'-trideoxy-lyxo-L-hexopyranose)-3-methoxycarbonyl-3-methyl-3,4,5,10-tetrahydro-5,10-dioxo-naphtho-[2,3-c] pyran (BCH-2076)**



BCH-2076

Step 1: (1'S, 1S, 3R)-1-(4'-p-nitrobenzoyl-3'-trifluoroacetamido-2',3',6'-trideoxy-lyxohexopyranose)-3-methoxy-carbonyl-3-methyl-5,8-dioxo-4,5,8-trihydro-1H-benzo-[2,3-c]-pyran

(1'S,1S,3R) 1-(2',3',6'-trideoxy-3-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose-5,8-dimethoxy-3-aceto-3-methylisochroman (62 mg, 0.0945 mmol) in acetonitrile (3 ml) was stirred at 0°C while a solution of ammonium cerium nitrate (165.5 mg, 0.284 mmol) in water (1.5 ml), pre-treated with sodium bicarbonate (15.1 mg, 0.18 mmol), was added dropwise. The solution was stirred for 5 minutes at 0°C then poured to water and extracted with dichloromethane. The organic layer was dried and evaporated to give desired titled product (40 mg, 0.064 mmol).

^{1}H NMR ($CDCl_3$ 250 MHz, Bruker): δ, 1.27 (3H, d, J = 6.5 Hz, 6'-CH_3), 1.57 (3H, s, 3-CCH_3), 1.91 (1H, dd, J = 11.8 Hz, 4.7 Hz, 2'-CH), 2.10 (1H, d tr, J = 11.8 Hz, 3.6 Hz, 2'-CH), 2.72 (1H, d, J = 17.9 Hz, 4-CH), 2.94 (1H, dd, J = 17.9 Hz, 0.9 Hz, 4-CH), 3.75 (3H, s, OCH_3), 4.54 (1H, m, 3'-CH), 4.64 (1H, qua, J = 6.5 Hz, 5'-CH), 5.40 (1H, s, 4'-CH), 5.65 (1H, d, J = 2.4 Hz, 1'-CH), 6.06 (1H, s, 1-CH), 6.52 (1H, d, J = 8.2 Hz, $NHCOCF_3$), 6.77 (1H, d, J = 10 Hz, Quin-H), 6.83 (1H, d, J = 10Hz, Quin-H), 8.27 (4H, m, PNB).

IR (Nicolet, 205 FT, film on NaCl plate): cm^{-1}, 3336.1, 3083.4, 2956.1, 2849.7, 1734.5, 1664.2, 1529.4, 1352.7, 1272.9, 1162.7, 989.8, 949.9, 839.70, 721.95.

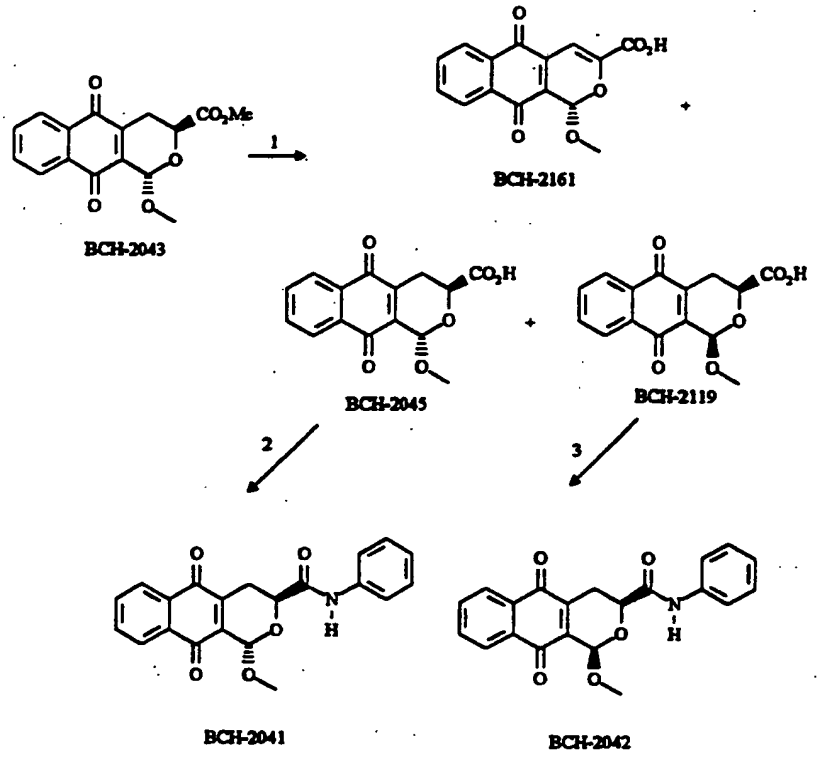
Step 2: (1'S, 1S, 3R)-1-(4'-p-nitrobensoyl-3'-trifluoroacetamido-2',3',6'-trideoxy-lyxohexopyranose)-3-methoxy-carbonyl-3-methyl-5,10-dioxo-4,5,10-trihydro-1H-naphtho-[2,3-c]-pyran

The titled compound was obtained as per procedure described in step 2, example 5, but using the quinone from step 1 herein.
^1H NMR ($CDCl_3$ 250 MHz, Bruker): δ, 1.32 (3H, d, J = 6.6 Hz, 6'-CH_3), 1.95 (1H, dd, J = 12.4 Hz, 5.0 Hz, 2'-CH), 2.10 (1H, d tr, J = 12.4 Hz, 3.5 Hz, 2'-CH), 2.88 (1H, d, J = 18.2 Hz, 4-CH), 3.13 (1H, dd, J = 18.2 Hz, 1.0 Hz, 4-CH), 3.75 (3H, s, OCH_3), 4.56 (1H, m, 3'-CH), 4.76 (1H, qua, J = 6.6 Hz, 5'-CH), 5.45 (1H, s, 4'-CH), 5.72 (1H, d, J = 2.0 Hz, 1'-CH), 6.26 (1H, s, 1-CH), 6.45 (1H, d, J = 7.1 Hz, $NHCOCF_3$), 7.78 (2H, m, 7, 8-ArH), 8.12 (2H, m, 6, 9-ArH), 8.29 (4H, m, PNB). IR (Nicolet, 205 FT, film on NaCl plate): cm^{-1}, 3329.3, 2955.6, 2926.9, 2855.3, 1732.9, 1709.5, 1668.3, 1596.8, 1532.3, 1349.5, 1272.6, 1217.6, 1184.7, 1164.1, 996.5, 952.5, 729.90, 720.30.

Step 3: (1'S, 1S, 3R)-1-(3'-trifluoroacetamido-2',3',6'-trideoxy-L-lyxohexopyranose)-5,10-dioxo-4,5,10-trihydro-1H-naphtho-[2,3-c]-pyran (BCH-2076)

The titled compound was obtained from the glycoside from step 2 herein via base hydrolysis as per procedure described in step 3, example 5.
^1H NMR ($CDCl_3$, 250 MHz, Bruker): δ, 1.38 (3H, d, J = 6.0 Hz, 6'-CH_3), 1.60 (3H, s, 3-CCH_3), 1.85 (1H, d, J = 6.8 Hz, 4'-OH), 1.85 (1H, dd, J = 9.4 Hz, 2.6 Hz, 2'-HCH_a), 1.96 (1H, d, J = 9.4 Hz, 2'-HCH_e), 2.87 (1H, d, J = 18.8 Hz, 4-HCH_a), 3.12 (1H, dd, J = 18.8 Hz, 0.6 Hz, 4-HCH_e), 3.63 (1H, br d, J = 6.8 Hz, 4'-CH), 3.75 (3H, s, OCH_3), 4.28 (1H, qua, J = 8.8 Hz, 3'-CH), 4.55 (1H, qua, J = 6.0 Hz, 5'-CH), 5.54 (1H, s, 1'-CH), 6.21 (1H, s, 1-CH), 6.71 (1H, br d, J = 9.4 Hz, $NHCOCF_3$), 7.75 (2H, m, 7, 8-ArH), 8.11 (2H, m, 6, 9-ArH),
IR (Nicolet , 205 FT, film on NaCl plate): cm^{-1}, 3420.1 (br str), 2955.6, 1718.7, 1668.3, 1595.5, 1377.3, 1329.7, 1287.7, 1161.8, 982.68, 921.12, 730.64.

Example 49: (1,3-trans)-anline-(1-methoxy-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran)-3-carboxamide (BCH-2041) and (1,3-cis)-anline-(1-methoxy-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran)-3-carboxamide (BCH-2042)



Step 1:

The compound from step 3, example 16, (21 mg, 0.0695 mmol) was dissolved in acetonitrile (10 ml) and then cooled to 0°C. NaOH (0.1 N, 1.4 ml, 0.14 mmol) solution was then added slowly. After 10 minutes, the brown solution was poured to water, extracted with ethyl acetate. The aqueous layer was acidified with dilute HCl and extracted with ethyl acetate. The organic layer containing acid was dried and evaporated to give a mixture of 3 products (18 mg). Chromatography ($CHCl_3$/MeOH/HOAc = 100:15:2) allowed separation of the 3 compounds. One of the products was the same as the one obtained in step 6, example 16, and had: ^1H NMR (CD_3COCD_3, 250 MHz, Bruker): δ, 3.58 (3H, s, OCH_3), 6.36 (1H, s, 1-CH), 7.22 (1H, s, 4-CH), 7.91 (2H, m, 7, 8-ArH), 8.12 (2H, m, 6, 9-ArH).

The second product (1,3-trans)-1-methoxy-3-carboxyl-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran, BCH-2045 had:
^1H NMR (CD_3SOCD_3 250 MHz, Bruker): δ, 2.55 (1H, dd, J = 18.5 Hz, 12.4 Hz, 4-HCH_a), 2.88 (1H, dd, J = 18.5 Hz, 3.5 Hz, 4-HCH_e), 3.47 (3H, s, OCH_3), 4.49 (1H, dd, J = 12.4 Hz, 3.5 Hz, 3-CH), 5.55 (1H, s, 1-CH), 7.88 (2H, m, 7, 8-ArH), 8.00 (2H, m, 6, 9-ArH).
IR (Nicolet , 205 FT, film on NaCl plate): cm^{-1}, 3549.2-3183.8, 2922.8, 1722.1, 1289.0, 1107.4, 1012.3, 951.08, 808.9, 793.5.
The third product: (1,3-cis)-1-methoxy-3-carboxyl-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran, (BCH-2119), had:
^1H NMR (CD_3SOCD_3 250 MHz, Bruker): δ, 1.28 (1H, dd, J = 15.3 Hz, 11.5 Hz, 4-HCH_a), 2.58 (1H, dd, J = 11.5 Hz, 2.9 Hz, 4-HCH_e), 3.45 (3H, s, OCH_3), 4.17 (1H, dd, J = 11.5 Hz, 2.9 Hz, 3-CH), 5.62 (1H, s, 1-CH), 7.89 (4H, m, 6, 7, 8, 9-ArH).

Step 2: (1,3-trans)-1-methoxy-3-N-anilinylcarbonyl-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran, BCH-2041:

A solution of acid from step 1 herein (20 mg, 0.069 mmol) in THF (4 ml) was cooled to 0°C. To the solution was added DMF (1 µl, as a catalyst) and then oxalyl chloride (12 µl, 0.138 mmol). The mixture was stirred at 0°C for 45 minutes and at room temperature for 20 minutes. Solvent was evaporated. The residue was redissolved in methylene chloride and then evaporated. The residue was dissolved again in methylene chloride (4 ml) and half of the volume was taken for coupling with aniline (4 µl, 0.044 mmol) as follows: To the ice-cold solution of the acid chloride was added aniline (1 eq.) in 1 ml of methylene chloride. The reaction mixture was stirred for 10 minutes. It was poured to water and extracted with methylene chloride. The organic layer was dried and evaporated to give a crude product which was purified by recrystallization from methylene chloride and hexane. The desired titled product was obtained (11 mg) as a light yellow solid.
M.P. 183-184°C.
^1H NMR ($CDCl_3$, 250 MHz, Bruker): δ, 2.63 (1H, dd, J = 19.4 Hz, 12.5 Hz, 1-HCH_a), 3.30 (1H, dd, J = 19.3 Hz, 4.2 Hz, 1-HCH_e), 3.67 (3H, s, OCH_3), 4.74 (1H, dd, J = 12.5 Hz, 4.5 Hz, 3-CH), 5.77 (1H, s, 1-CH), 7.16 (1H, tr, J = 8.5 Hz, 4'-Ani-H), 7.47 (2H, tr, J = 8.5 Hz, 3', 5'-Ani-H), 7.52 (2H, d, J = 8.5 Hz, 2', 6'-Ani-H), 7.75 (2H, m, 7, 8-ArH), 8.10 (2H, m, 6, 9-ArH), 8.31 (1H, s, NHCO).

IR (Nicolet , 205 FT, film on NaCl plate): cm^{-1}, 3278.8, 2923.0, 1665.0, 1593.4, 1533.0, 1445.7, 1798.0, 1060.7, 960.0, 755.6, 688.2, 679.0.

Step 3: (1,3-cis)-1-methoxy-3-N-anilinylcarbonyl-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran, BCH-2042,

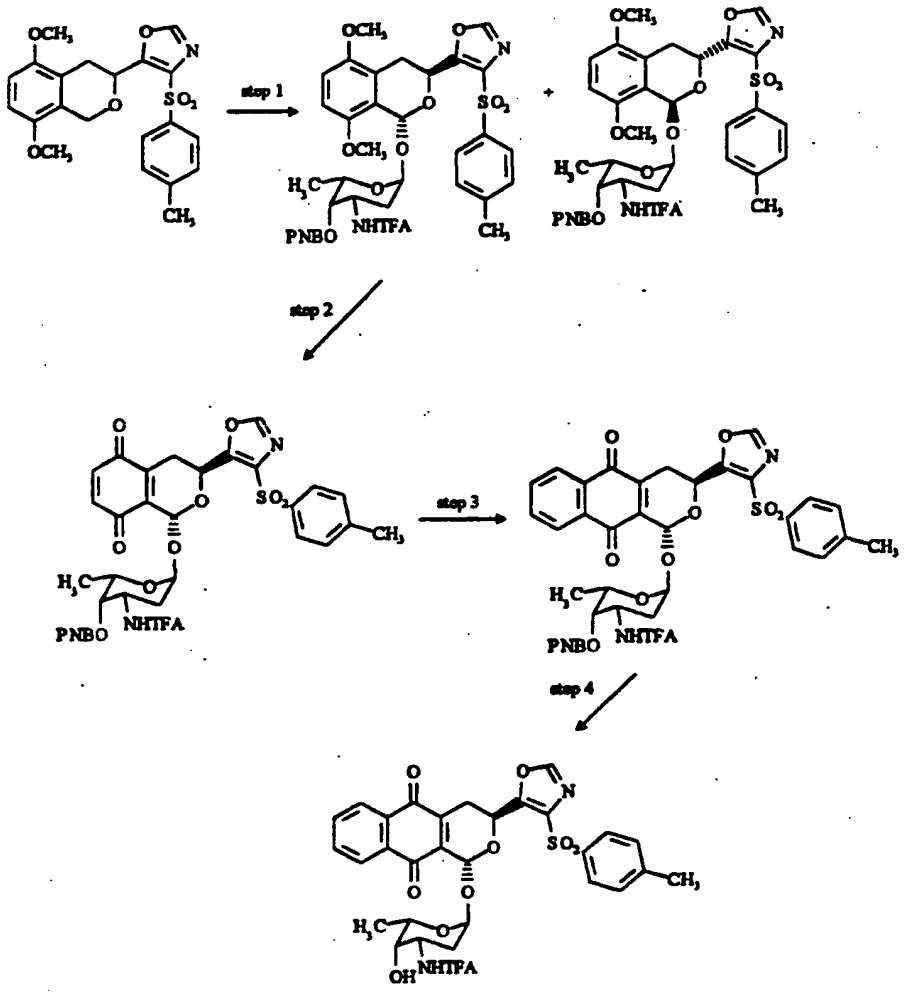
A similar to the procedure described previously in step 2, the cis acid from step 1 herein was converted to the titled product.

M.P. 217-219°C.

^1H NMR ($CDCl_3$, 250 MHz, Bruker): δ, 2.49 (1H, dd, J = 15.6 Hz, 11.2 Hz, 4-HCH_a), 3.08 (1H, dd, J = 15.6 Hz, 3.2 Hz, 4-HCH_e), 3.65 (3H, s, OCH_3), 4.50 (1H, dd, J = 11.2 Hz, 3.2 H, 3-CH), 5.94 (1H, s, 1-CH), 7.14 (1H, tr, J = 7.6 Hz, p-Ani-H), 7.35 (2H, tr, J = 7.6 Hz, m-Ani-H), 7.56 (2H, d, J = 7.6 Hz, O-Ani-H), 7.78 (2H, m, 7, 8-ArH), 8.00 (2H, m, 6, 9-ArH), 8.21 (1H, s, NHCO).

IR (Nicolet , 205 FT, film on NaCl plate): cm^{-1}, 3353.5, 3052.9, 2928.1, 2853.9, 1694.6, 1597.5, 1531.8, 1443.3, 1300.6, 1172.1, 1117.8, 1060.7, 1043.6, 1026.5, 906.7, 750.6, 712.5, 692.6.

Example 50: Preparation of (1'S,1R,3S)-1-(3'-trifluoroacetamido-2',3',6'-trideoxy-lyxohexpyranose)-3-(5"-tosyloxazolyl)-3,4,5,10-tetrahydro-5,10-dioxo-naphtho-[2,3-c] pyran (BCH-2150)



BCH-2150

Step 1: (1'S, 1S, 3R)-1-(4'-p-nitrobenzoyl-2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3-(5"-tosyloxazolyl)-5,8-dimethoxy isochroman

To the compound from step 4, example 47, (50 mg, 0.120 mmol) in dichloromethane (15 ml) stirred with 5'-p-nitrobenzoyl-3',4',7'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose (49 mg, 0.125 mmol) was added 1,2-dichloro-4,5-dicyano-benzoquinone (35.6 mg, 0.157 mmol). The resulting mixture was stirred for 18 hours at 40°C. Solvent was evaporated and the crude product was chromatographed (hexane/ethyl acetate=3/2) to give the titled compound (17 mg) and the (1'S,1R,3S) diastereomer (12 mg).

The titled compound had:

^{1}H NMR (acetone-d_6, 250 MHz, Bruker): δ, 1.27 (3H, d, J = 5.9 Hz, 6'-CH_3), 2.14-2.30 (2H, m, 2'-CH_2), 2.44 (3H, s, tosyl-CH_3), 3.01 (2H, d, J

= 6.5 Hz, 4-CH_2), 3.82 (3H, s, OCH_3), 3.92 (3H, s, OCH_3), 4.65 (1H, m, 3'-CH), 4.86 (1H, qua, J = 5.9 Hz, 5'-CH), 5.71 (1H, d, J = 2.4 Hz, 4-CH), 6.17 (1H, tr, J = 6.5 Hz, 3-CH), 6.24 (1H, s, 1-CH), 6.95 (2H, m, 6, 7-ArH), 7.48 (2H, d, J = 7.4 Hz, 3",5"-tosyl-H), 7.95 (2H, d, J = 7.4 Hz, 2", 6"-tosyl-H), 8.38 (4H, m, PNB), 8.37 (1H, s, oxa-H), 8.66 (1H, d, J = 7.4 Hz, $NHCOCF_3$).

The (1'S, 1R, 3S)-1-(4'-p-nitrobenzoyl-2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3-(5"-tosyloxa-zolyl)-5,8-dimethoxy isochroman had:

^1H NMR (acetone-d_6, 250 MHz, Bruker): δ, 0.80 (3H, d, J = 6.8 Hz, 6'-CH_3), 2.19 (1H, m, 2'-HCH_a), 2.48 (1H, d tr, J = 11.8 Hz, 4.1 Hz, 2'-HCH_e), 2.46 (3H, s, tosyl-CH_3), 2.88 (1H, dd, J = 17.6 Hz, 11.8 Hz, 4-HCH_a), 3.04 (1H, dd, J = 17.6 Hz, 4.4 Hz, 4-HCH_e), 3.83 (3H, s, OCH_3), 3.86 (3H, s, OCH_3), 4.42 (1H, qua, J = 6.8 Hz, 5'-CH), 4.84 (1H, m, 3'-CH), 5.48 (1H, s, 4'-CH), 5.58 (1H, d, J = 3.5 Hz, 1'-CH), 6.01 (1H, s, 1-CH), 6.92 (1H, d, J = 6.5 Hz, ArH), 6.96 (1H, d, J = 6.5 Hz, ArH), 7.54 (2H, d, J = 9.1 Hz, 3", 5"-tosyl-H), 8.06 (2H, d, J = 9.1 Hz, 2", 6"-tosyl-H), 8.35 (1H, s, oxa-H), 8.49 (4H, m, PNB), 8.62 (1H, d, J = 6.8 Hz, $NHCOCF_3$).

Step 2: (1'S, 1S, 3R)-1-(4'-p-nitrobenzoyl-2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3-(5"-tosyloxazolyl)-5,8-dioxo-3,4,5,8-tetrahydrobenzo-[2,3-c]-pyran.

The compound from step 1 herein (17 mg, 0.021 mmol) in acetonitrile (2 ml) was cooled to 0°C and ammonium cerium nitrate (35.5 mg, 0.0648 mmol, pretreated with sodium bicarbonate, 3.6 mg, 0.042 mmol) was added dropwise. The reaction mixture was stirred for 15 minutes at 0°C then poured to water. It was extracted with dichloromethane. The organic phase was washed with brine, dried (over sodium sulfate) and evaporated to give a crude product which was purified on silica gel (hexane/EtOAc = 2:1) to give the desired titled product (7 mg).

^1H NMR (acetone-d_6, 250 MHz, Bruker): δ, 1.04 (3H, d, J = 6.5 Hz, 6'-CH_3), 2.12-2.35 (2H, m, 2'-CH_2), 2.45 (3H, s, tosyl-CH_3), 2.80-2.93 (2H, m, 4-CH_2), 4.55 (1H, qua, J = 6.5 Hz, 5'-CH), 4.86 (1H, m, 3'-CH), 5.49 (1H, s, 4'-CH), 5.61 (1H, d, J = 2.1 Hz, 1'-CH), 5.85 (1H, s, 1-CH), 6.12 (1H, dd, J = 10.6 Hz, 4.7 Hz, 3-CH), 6.80 (1H, d, J = 10.6 Hz, Quin-H), 6.85 (1H, d, J = 10.6 Hz, Quin-H), 7.48 (2H, d, J = 8.8 Hz, 3",

5"-tosyl-H), 7.88 (1H, s, oxa-H), 7.94 (2H, d, J = 8.8 Hz, 2", 6"-tosyl-H), 8.28 (4H, m, PNB).

Step 3: (1'S, 1R, 3S)-1-(4'-p-nitrobensoyl-3-trifluoroacetamido-2',3',6'-trideoxy-L-lyxohexopyranose)-3-(5"-tosyl-oxasolyl)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran

The compound from step 2 herein (9 mg, 0.012 mmol) was stirred with 1-acetoxy-1,3-butadiene (28 µl, 0.236 mmol) in toluene (4 ml) and THF (0.5 ml) at 50°C for 18 hours. Solvent was evaporated and the crude product was chromatographed (toluene/ethyl acetate = 5/1) to give the desired titled product (4.8 mg).

^{1}H NMR ($CDCl_3$ 250 MHz, Bruker): δ, 1.06 (3H, d, J = 6.2 Hz, 6'-CH_3), 2.00 (1H, d tr, J = 11.5 Hz, 2.9 Hz, 2'-HCH_a), 2.25 (1H, dd, J = 11.5 Hz, 4.4 Hz, 2'-HCH_e), 2.44 (3H, s, tosyl-CH_3), 2.98 (1H, d, J = 5.6 Hz, 4-CH), 2.99 (1H, d, J = 11.0 Hz, 4-CH), 4.60 (1H, qua, J = 6.2 Hz, 5'-CH), 4.87 (1H, m, 3'-CH), 5.40 (1H, s, 4'-CH), 5.72 (1H, d, J = 2.0 Hz, 1'-CH), 6.05 (1H, s, 1-CH), 6.19 (1H, dd, J = 11.0 Hz, 5.6 Hz, 3-CH), 6.66 (H, d, J = 6.5 Hz, $NHCOCF_3$), 7.49 (2H, d, J = 8.8 Hz, 3", 5"-tosyl-H), 7.79 (2H, m, 7, 8-ArH), 7.90 (1H, s, oxa-H), 7.95 (2H, d, J = 8.8 Hz, 2", 6"-tosyl-H), 8.13 (2H, m, 6, 9-ArH), 8.31 (4H, m, PNB).

Step 4: (1'S, 1R, 3S)-2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose-3-[5'-tosyloxasolyl]-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran (BCH-2150)

To the compound from step 3 herein (4.8 mg, 5.92 mmol) in THF (0.5 ml) and methanol (1.5 ml) cooled to 0°C was added sodium methoxide (4.37 M,1.4 µl, 5.92 mmol). After 5 minutes, the reaction was quenched with dilute hydrochloride acid and extracted with methylene chloride. The organic layer was dried (over Na_2SO_4) and evaporated to give a crude product which was purified on TLC ($CHCl_3$:MeOH = 100:7) to give desired titled product as an off-white solid (1.3 mg).

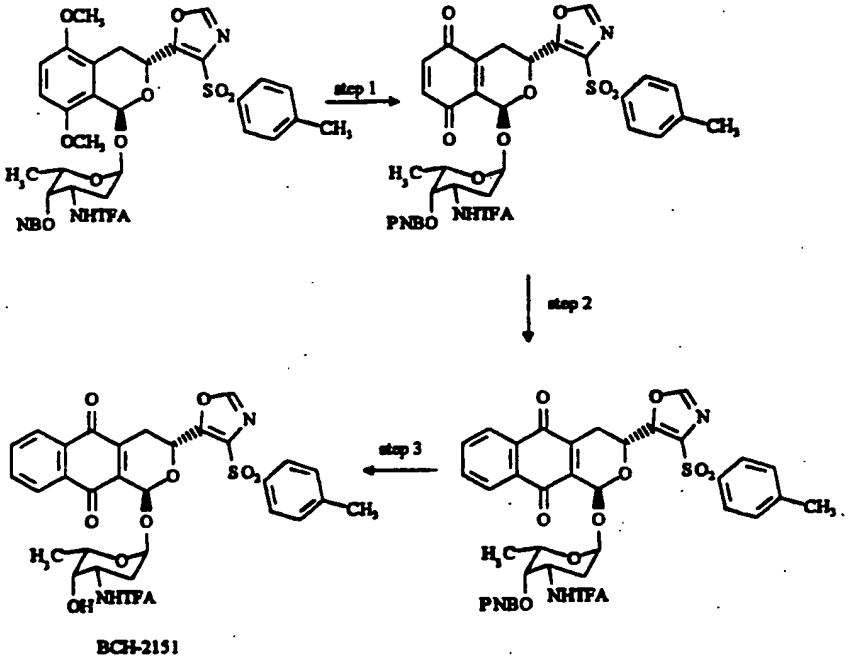
M.P. 130-135°C.

^{1}H NMR ($CDCl_3$, 250 MHz, Bruker): δ, 1.13 (3H, d, J = 6.5 Hz, 6'-CH_3), 1.78 (1H, tr d, J = 11.2 Hz, 2'-HCH_a), 2.05 (1H, m, 2'-HCH_e, due to solvent overlap, this is an estimation), 2.43 (3H, s, tol-CH_3), 2.92 (1H, d, J = 5.9 Hz, 4-HCH_a), 2.94 (1H, d, J = 10.5 Hz, 4-HCH_e), 3.71 (1H, m, 4'-OH), 4.20 (1H, dd, J = 5.9 Hz, 3-2 Hz, 4'-OH), 4.47 (1H, qua,

J = 6.5 Hz, 5'-CH_3), 4.58 (1H, m, 3'-CH), 5.55 (1H, d, J = 3.0 Hz, 1'-CH), 5.99 (1H, s, 1-CH), 6.16 (1H, dd, J = 10.6 Hz, 5.9 Hz, 3-CH), 6.77 (1H, d, J = 10.6 Hz, $NHCOCF_3$), 7.36 (2H, d, J = 8.8 Hz, tosyl-H), 7.79 (2H, m, 7, 8-ArH), 7.90 (1H, s, oxa-H), 7.91 (2H, d, J = 8.8 Hz, tosyl-H), 8.11 (2H, m, 6, 9-ArH).

IR (Nicolet 205 FT, film on NaCl plate): cm^{-1}, 3379.1, 2956.4, 2927.8, 2854.7, 1716.9, 1669.3, 1335.6, 1297.4, 1148.0, 985.2.

Example 51: **Preparation of (1'S,1S,3R)-1-(3'trifluoroacetamido-2',3',6'-trideoxy-lyxo-L-hexopyranose)-3-(5"-tosyloxasolyl)-3,4,5,10-tetrahydro-5,10-dioxo-naphtho-[2,3-c] pyran (BCH-2151)**



Step 1: **(1'S, 1S, 3R)-1-(4'-p-nitrobenzoyl-2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3-(5"-tosyloxasolyl)-5,8-dioxo-3,4,5,8-tetrahydrobenzo-[2,3-c]-pyran**

Starting with the (1'S,1S,3R) diastereomer from step 1, example 50, (12 mg, 0.015 mmol), using the same materials (ammonium cerium nitrate, 25 mg, 0.046 mmol; $NaHCO_3$, 2.55 mg, 0.0304 mmol; acetonitrile, 1.5 ml; H_2O, 0.4 ml) and following the same procedures as described in step 2, example 50, the desired titled product was obtained (9 mg).

^1H NMR (acetone-d_6, 250 MHz, Bruker): δ, 1.27 (3H, d, J = 6.6 Hz, 6'-CH_3), 2.20 (2H, m, 2'-CH_2), 2.45 (3H, s, tosyl-CH_3), 2.95 (1H, d, J = 6.8 Hz, 4-CH), 2.95 (1H, d, J = 8.8 Hz, 4-CH), 4.56 (1H, m, 3'-CH), 4.74 (1H, qua, J = 6.6 Hz, 5'-CH), 5.53 (1H, s, 4'-CH), 5.68 (1H, d, J = 2.9 Hz, 1'-CH), 6.01 (1H, s, 1-CH), 6.09 (1H, dd, J = 8.8 Hz, 6.8 Hz, 3-CH), 6.93 (1H, d, J = 11.8 Hz, Quin-H), 6.96 (1H, d, J = 11.8 Hz, Quin-H), 7.49 (2H, d, J = 8.8 Hz, 3", 5"-tosyl-H), 7.93 (2H, d, J = 8.8 Hz, 2", 6"-tosyl-H), 8.36 (1H, s, oxa-H), 8.39 (4H, m, PNB), 8.68 (1H, d, J = 8.8 Hz, $NHCOCF_3$).

Step 2: **(1'S, 1S, 3R)-1-(4'-p-nitrobenzoyl-3-trifluoroacetamido-2',3',6'-trideoxy-L-lyxohexopyranose)-3-(5"-tosyl-oxazolyl)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran**

The compound from step 2 herein (7 mg, 0.009 mmol) was reacted with 1-acetoxy-1,3-butadiene (21 µl, 0.184 mmol) in toluene (3 ml) at 50°C for 18 hours. The solvent was evaporated to give a crude product. After chromatography (toluene/ethyl acetate = 5:1) desired titled product was obtained (6.4 mg).

^1H NMR ($CDCl_3$ 250 MHz, Bruker): δ, 1.34 (3H, d, J = 7.1 Hz, 6'-CH_3), 2.15 (1H, d tr, J = 12.9 Hz, 4.1 Hz, 2'-HCH_a), 2.32 (1H, dd, J = 12.9 Hz, 4.1 Hz, 2'-HCH_e), 2.45 (3H, s, tosyl-CH_3), 2.96 (1H, dd, J = 18.2 Hz, 4.1 Hz, 4-HCH_a), 3.13 (1H, dd, J = 18.2 Hz, 11.2 Hz, 4-HCH_e), 4.64 (1H, m, 3'-CH), 4.77 (1H, qua, J = 7.1 Hz, 5'-CH), 5.52 (1H, s, 4'-CH), 5.76 (1H, d, J = 2.0 Hz, 1'-CH), 6.08 (1H, dd, J = 11.2 Hz, 4.1 Hz, 3-CH), 6.20 (1H, s, 1-CH), 6.21 (1H, m, $HNCOCF_3$), 7.37 (2H, d, J = 8.2 Hz, 3", 5"-tosyl-H), 7.71 (2H, m, 7, 8-ArH), 7.89 (2H, d, J = 8.2 Hz, 2", 6"-tosyl-H), 7.90 (1H, s, oxa-H), 8.15 (1H, m, 6, 9-ArH), 8.31 (4H, m, PNB).

Step 3: **(1'S, 1S, 3R)-2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose-3-[5'-tosyloxazolyl)]-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-C]-pyran (BCH-2151)**

To PNB derivative from step 2 herein (6.4 mg, 0.0079 mmol) stirred in tetrahydrofuran (0.5 ml) and methanol (1.5 ml) at 0°C was added sodium methoxide (4.373 M, 1.8 µl, 0.0079 mmol). After 5 minutes, the pink solution was quenched with dilute HCl. The product was extracted with methylene chloride. The organic layer was dried and evaporated to give

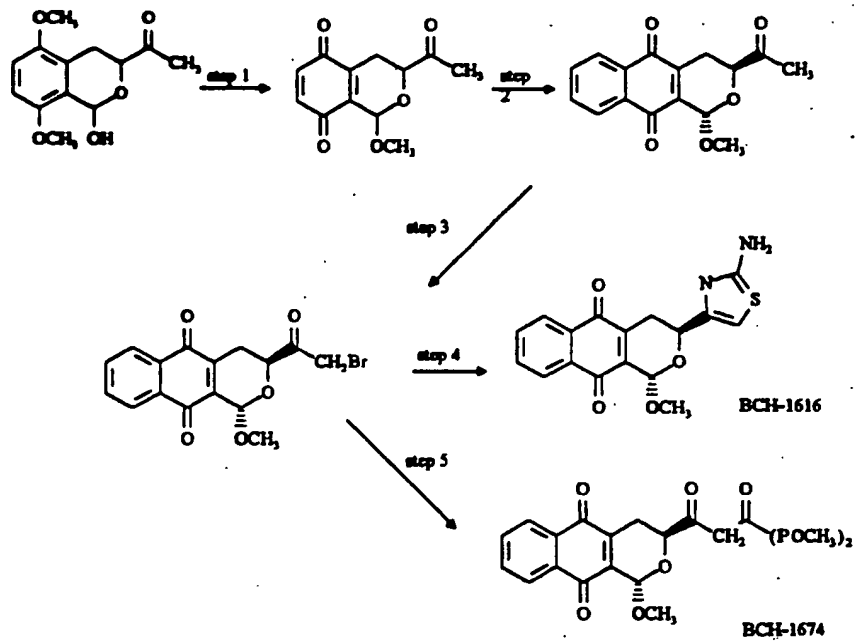
a crude product which was purified by thin-layer-chromatography ($CHCl_3$:MeOH = 100:7) to desired titled product as an off-white solid (0.8 mg).

M.P. 100-105°C.

^1H NMR ($CDCl_3$, 250 MHz, Bruker): δ, 1.41 (3H, d, J = 5.9 Hz, 6'-CH_3), 1.92 (1H, tr d, J = 11 Hz, 3.5 Hz, 2'-HCH_a, estimation), 2.20 (1H, m, 2'-HCH_e, estimation), 2.44 (3H, s, tol-CH_3), 2.95 (1H, dd, J = 18.5 Hz, 4.7 Hz, 4-HCH_e), 3.12 (1H, dd, J = 18.5 Hz, 11.2 Hz, 4-HCH_a), 4.00 (1H, m, 4'-CH), 4.37 (m, 1H, 3'-CH), 4.60 (1H, qua, J = 5.9 Hz, 5'-CH), 5.10 (1H, br s, 4'-OH, estimation), 5.58 (1H, d, J = 3.5 Hz, 1'-CH), 6.05 (1H, dd, J = 11.2 Hz, 4.7 Hz, 3-CH), 6.15 (1H, s, 1-CH), 6.66 (1H, m, $NHCOCF_3$), 7.36 (2H, d, J = 8.8 Hz, tosyl-H), 7.78 (2H, m, 7, 8-ArH), 7.87 (1H, s, oxa-H), 7.88 (2H, d, J = 8.8 Hz, tosyl-H), 8.12 (2H, m, 6, 9-ArH).

IR (Nicolet 205 FT, film on NaCl plate): cm^{-1}, 3368.3 2961.8, 2930.2, 2848.9, 1715.0, 1669.9, 1463.0, 1332.8, 1289.0, 1153.4, 975.46.

Example 52: Preparation of (1,3-trans)-1-methoxy-3-(3'-aminothiazolyl)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho [2,3-c]-pyran (BCH-1616) and (1,3-trans)-1-methoxy-3-dimethoxyphosphonoacetyl-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho [2,3-c]-pyran (BCH-1674)



Step 1: 1-methoxy-3-acetyl-5,8-dioxo-3,4,5,8-tetrahydrobenzo-[2,3-c]-pyran

A sample of 5,8-dimethoxy-1-hydroxy-3-acetoisochroman (200 mg, 0.79 mmol) in MeOH (10 ml) was stirred at room temperature while a solution of CAN (2.16 g, 3.95 mmol) in water (9 ml) was added dropwise. After 5 minutes, the reaction mixture was poured to water and then extracted with methylene chloride. The organic layer was dried (over sodium sulfate), and evaporated to give a yellow sticky solid (157 mg). ^{1}H NMR showed that desired titled product was obtained with 89% purity.
^{1}H NMR ($CDCl_3$, 250 MHz Bruker), δ: 2.28 (s, 3H, $COCH_3$), 2.35 (dd, 1H, J = 20.5 Hz, 12.1 Hz, 4-Ha), 2.78 (dd, 1H, J = 20.5 Hz, 4.3 Hz, 4-He), 3.56 (s, 3H, OCH_3), 4.44 (dd, 1H, J = 12.1 Hz, 4.3 Hz, 3-H), 5.46 (s, 1H, 1-H), 6.73 (m, 2H, 6.7-quinone).

Step 2: 1-methoxy-3-acetyl-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran

The bicyclic quinone from step 1 herein (157 mg, 0.66 mmol) was stirred with 1-acetoxy-1,3-butadiene (632 µl, 5.32 mmol) in toluene (20 ml) at 40°C for 16 hours. Solvent was evaporated and the crude product was chromatographed (toluene:EtOAc = 100:25) to give desired titled tricyclic quinone as a yellow solid (190 mg).
M.P. 169.8-170.8°C.
^{1}H NMR ($CDCl_3$, 250 MHz Bruker), δ: 2.34 (s, 3H, $COCH_3$), 2.53 (dd, 1H, J = 20.7 Hz, 10.7 Hz, 4-Ha), 3.00 (dd, 1H, J = 10.7 Hz, 4.3 Hz, 4-He), 3.63 (s, 3H, OCH_3), 4.54 (dd, 1H, J = 10.7 Hz, 4.3 Hz, 3-H), 5.66 (s, 1H, 1-H), 7.73 (m, 2H, 7.8-ArH), 8.06 (m, 2H, 6.8-ArH).
IR (Nicolet 205 FT, film on NaCl plate), cm^{-1}: 2923.4, 2827.6, 1717.7, 1668.2, 1637.3, 1597.1, 1368.3, 1331.3, 1300.3, 1281.8, 1179.8, 1105.6, 1083.9, 1046.8, 875.5, 799.8, 714.2, 686.1.

Step 3: 3-bromoacethyl-1-methoxy-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran

To a solution of product from step 2 herein (50 mg, 0.175 mmol) in THF (3 ml) at room temperature was added pyridinium hydrobromide perbromide (1.3 eq.) in THF (2 ml). The mixture was stirred for 45 minutes at room

temperature. It was poured to water and extracted with methylene chloride. The organic layer was dried and evaporated to give a product. TLC and ^1H NMR both showed that the desired titled product (76 mg) was obtained with purity >90%.

M.P. 169.8-170.8°C.

^1H NMR ($CDCl_3$, 250 MHz Bruker), δ: 2.53 (dd, 1H, J = 20.3 Hz, 11.0 Hz, 4-Ha), 3.02 (dd, 1H, J = 20.3 Hz, 4.1 Hz, 4-He), 3.64 (s, 3H, OCH_3), 4.15 (d, 1H, J = 12.7 Hz, $BrCH_AH$), 4.35 (d, 1H, J = 12.7 Hz, Br CHH_B), 4.84 (dd, 1H, J = 11.0 Hz, 4.1 Hz, 3-H), 5.65 (s, 1H, 1-H), 7.72 (m, 2H, 7.8-ArH), 8.02 (m, 2H, 6.9-ArH).

Step 4: (1,3-trans)-1-methoxy-3-(3'-aminothiazolyl)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho [2,3-c] pyran (BCH-1616)

Bromomethyl ketone from step 3 herein (20 mg, 0.054 mmol) was stirred with thiourea at room temperature for 3.5 hours in ether (2 ml) and dichloromethane (2 ml). It was poured to sat. sodium bicarbonate and extracted with dichloromethane. The organic layer was evaporated to give crude product which was chromatographed (MeOH:$CHCl_3$:HOAc = 4:100:1) to give desired titled product (5.3 mg). A polar by-product was also obtained (8 mg).

^1H NMR ($CDCl_3$, 250 MHz Bruker), δ: 2.77 (1H, dd, J = 18.8 Hz, 11.8 Hz, 4-HCH_a), 3.00 (1H, dd, J = 18.8 Hz, 5.2 Hz, 4-HCH_e), 3.63 (3H, s, OCH_3), 5.03 (1H, dd, J = 11.8 Hz, 5.2 Hz, 3-CH), 5.67 (1H, s, 1-CH), 6.53 (1H, s, thia-H), 7.73 (2H, m, 6, 9-ArH), 8.08 (2H, m, 7, 8-ArH).

IR (Nicolet 205 FT, film on NaCl plate), cm^{-1}: 3429.8, 3346.7, 3130.7, 2957.8, 2921.3, 2854.8, 1664.9, 1641.6, 1591.7, 1521.9, 1455.5, 1408.9, 1327.1, 1294.1, 1102.0, 1039.9, 731.92, 708.07.

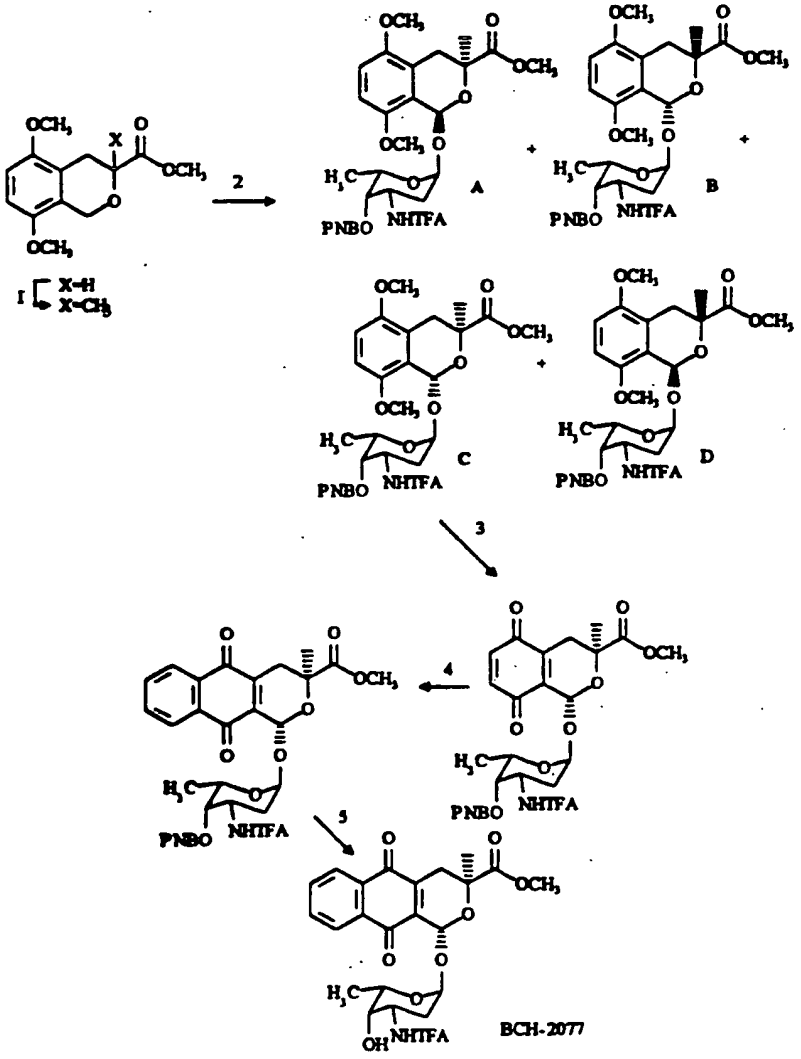
Step 5: 1-methoxy-3-dimethyl phosphonoacetyl-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran (BCH-1674)

A solution of bromomethylketone from step 3 herein (10 mg, 0.027 mmol) was refluxed with trimethylphosphite (3.54 µl, 0.03 mmol) and sodium iodide (0.2 mg, 0.05 mmol) in THF at 70°C overnight. Solvent was evaporated and the brown residue was chromatographed ($CHCl_3$:MeOH 50:1) to give desired titled product as a light-colored solid (2 mg).

^1H NMR ($CDCl_3$, 250 MHz, Bruker): δ, 2.60 (1H, dd, J = 19.8 Hz, 11.6 Hz 4-HCH_a), 2.94 (1H, dd, J = 19.8 Hz, 3.5 Hz, 4-H_eCH), 3.62 (3H, s, 1-

OCH_3), 3.85 (3H, s, $POCH_3$), 3.88 (3H, s, $POCH_3$), 4.59 (1H, dd, J = 11.6 Hz, 3.5 Hz, 3-CH), 5.02 (1H, br s, CHP), 5.15 (1H, br s, CHP), 5.62 (1H, s, 1-CH), 7.73 (2H, m, 6, 9-ArH), 8.08 (2H, m, 7, 8-ArH).

Example 53: **Preparation of (1'S,1R,3S)-1-(3'-trifluoroacetamido-2',3',6'-trideoxy-L-lyxohexopyranose)-3-methoxycarbonyl-3-methyl-3,4,5,10-tetrahydro-5,10-dioxo-1H-naphtho-[2,3-c] pyran (BCH-2077)**



Step 1: **3-methoxycarbonyl-3-methyl-5,8-dimethoxy isochroman**

A solution of di-isopropylamine (616.8 µl, 4.37 mmol) in THF (10 ml) was cooled to 0°C and degassed briefly. n-Butyl lithium (1.6 M in hexane, 2.60 ml, 4.17 mmol) was added. After stirred for 30 minutes at 0°C, the

solution was further cooled to -78°C. A solution of 5,8-dimethoxy-3-methoxycarbonylisochroman (1.0 g, 3.97 mmol) in THF (10 ml), pre-degassed, was added slowly. The resulting yellow solution was stirred for 1 hour at -78°C before the addition of methyliodide (1.01 ml, 16 mmol). After stirred further for 45 minutes, sat. NH_4Cl solution was added. The mixture was diluted with water and extracted with ethyl acetate. The organic layer was dried and evaporated to give a crude product which was chromatographed (hexane:EtOAc = 3:1) to give the desired product as a solid (650 mg, m p. 73.0-74.5°C) and another fraction (192 mg) which contained 66% of titled product and 34% of the starting material.

M.P. 73-74.5°C

^1H NMR ($CDCl_3$ 250 MHz, Bruker): δ, 1.50 (3H, s, 3-CCH_3), 2.58 (1H, d, J = 17.1 Hz, 4-CH), 3.25 (1H, d, J = 17.1 Hz, 4-CH), 3.64 (3H, s, OCH_3), 3.68 (3H, s, OCH_3), 3.72 (3H, s, OCH_3), 4.76 (1H, d, J = 17.1 Hz, 1-CH), 4.84 (1H, d, J = 17.1 H, 1-CH), 6.53 (1H, d, J = 7.1 Hz, ArH), 6.59 (1H, d, J = 7.1 Hz, ArH).

IR (Nicolet, 205 FT, film on NaCl plate): cm^{-1}, 2949.9, 2833.2, 1736.6, 1489.0, 1365.2, 1344.0, 1259.1, 1206.0, 1142.3, 1114.0, 1060.7, 295.7, 713.8.

Step 2: (1'S, 1R, 3S)-1-(4'-p-nitrobenzoyl-3'-trifluoroacetamido-2',3',6'-trideoxy-Llyxohexopyranose)-3-methoxy-carbonhyl-3-methyl-5,8-dimethoxy-isochroman.

The compound from step 1 herein (133 mg, 0.5 mmol) was reacted with DDQ (136 mg, 0.6 mmol) and 5'-p-nitrobenzoyl-3',4',7'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose (196 mg, 0.5 mmol) at 45°C for 16 hours, the same way as described in step 2, example 13. After chromatography (hexane:EtOAc = 2.5:1), four isomers were obtained: C, 49 mg; B, 24 mg; D, 73 mg; A, 56 mg.

For C, ^1H NMR ($CDCl_3$ 250 MHz, Bruker): δ, 1.22 (3H, d, J = 6.1 Hz, 6'-CH_3), 1.45 (3H, s, 3-CCH_3), 1.89 (1H, dd, J = 11.8 Hz, 4.7 Hz, 2'-CH), 2.05 (1H, d, tr, J = 11.8 Hz, 3.0 Hz, 2'-CH), 2.77 (1H, d, J = 17.1 Hz, 4-CH), 3.82 (1H, d, J = 17.1 Hz, 4-CH), 3.64 (3H, s, OCH_3), 3.78 (3H, s, OCH_3), 3.81 (3H, s, OCH_3), 4.52 (1H, m, 3'-CH), 4.60 (1H, qua, J = 6.1 Hz, 5'-CH), 5.42 (1H, s, 4'-CH), 5.74 (1H, d, J = 1.7 Hz, 1'-CH), 6.22 (1H, s, 1-CH), 6.36 (1H, d, J = 8.2 Hz, $NHCOCF_3$), 6.71 (1H, d, J = 8.8 Hz, ArH), 6.80 (1H, d, J = 8.8 Hz, ArH), 8.28 (4H, m, PNB).

IR (Nicolet, 205 FT, film on NaCl plate): cm^{-1}, 3328.4, 3077.3, 2946.4, 2843.8, 1740.1, 1527.9, 1492.5, 1259.1, 1114.0, 1054.2, 974.90, 947.90, 803.50, 716.80

The (1'S, 1S, 3S)-1-(4'-p-nitrobenzoyl-3'-trifluoroacetamido-2',3',6'-trideoxylyxohexopyranose)-3-methoxy-carbonyl-3-methyl-5,8-dimethoxy-isochroman had:

^1H NMR ($CDCl_3$ 250 MHz, Bruker): δ, 1.16 (3H, d, J = 7.3 Hz, 6'-CH_3), 1.63 (3H, s, 3-CCH_3), 2.02 (2H, m, 2'-CH_2), 2.86 (1H, d, J = 15.9 Hz, 4-CH), 3.21 (1H, d, J = 15.9 Hz, 4-CH), 3.65 (3H, s, OCH_3), 3.76 (6H, s, 2xOCH_3), 4.10 (1H, qua, J = 7.2 Hz, 5'-CH), 4.61 (1H, m, 3'-CH), 5.45 (1H, s, 4'-CH), 5.55 (1H, s, 1'-CH), 6.24 (1H, s, 1-CH), 6.68 (1H, d, J = 9.4 Hz, ArH), 6.76 (1H, d, J = 9.4 Hz, ArH), 6.23 (1H, s, $NHCOCF_3$), 8.26 (4H, m, PNB).

IR (Nicolet, 205 FT, film on NaCl plate): cm^{-1}, 3332.0, 2924.7, 2857.1, 1732.5, 1708.0, 1531.6, 1488.5, 1353.3, 1265.1, 1167.0, 957.18, 718.76.

The (1'S, 1S, 3R)-1-(4'-p-nitrobenzoyl-3'-trifluoroacetamido-2',3',6'-trideoxy-L-lyxohexopyranose)-3-methoxy-carbonyl-3-methyl-5,8-dimethoxy-isochroman had:

^1H NMR ($CDCl_3$ 250 MHz, Bruker): δ, 1.19 (3H, d, J = 6.1 Hz, 6'-CH_3), 1.60 (3H, s, 3-CCH_3), 1.87 (1H, dd, J = 12.4 Hz, 4.7 Hz, 2'-CH), 2.11 (1H, d tr, J = 12.4 Hz, 3.0 Hz, 2'-CH), 2.86 (1H, d, J = 16.5 Hz, 4-CH), 3.33 (1H, d, J = 16.5 Hz, 4-CH), 3.62 (3H, s,OCH_3), 3.78 (6H, s, 2xOCH_3), 4.54 (1H, qua, J = 6.1 Hz, 5'-CH), 4.57 (1H, m, 3'-CH), 5.41 (1H, s, 4'-CH), 5.69 (1H, d, J = 2.9 Hz, 1'-CH), 6.40 (1H, s, 1-CH), 6.45 (1H, d, J = 7.6 Hz, $NHCOCF_3$), 6.71 (1H, d, J = 8.9 Hz, ArH), 6.81 (1H, d, J = 8.9 Hz, ArH), 8.24 (4H, s, PNB).

IR (Nicolet, 205 FT, film on NaCl plate): cm^{-1}, 3325.5, 3077.2 2951.9, 2541.1, 1737.3, 1705.9, 1609.5, 1530.0, 1489.0, 1354.1, 1264.9, 970.9, 951.60, 804.80, 720.90.

The (1'S, 1R, 3R)-1-(4'-p-nitrobenzoyl-3'-trifluoroacetamido-2',3',6'-trideoxy-L-lyxohexopyranose)-3-methoxy-carbonyl-3-methyl-5,8-dimethoxy-isochroman had:

^1H NMR ($CDCl_3$ 250 MHz, Bruker): δ, 1.20 (3H, d, J = 6.0 Hz, 6'-CH_3), 1.53 (3H, s, 3-CCH_3), 1.93 (1H, dd, J = 11.8 Hz, 2.9 Hz, 2'-CH), 2.05 (1H, m, 2'-CH), 2.60 (1H, d, J = 16.5 Hz, 4-CH), 3.39 (1H, d, J = 16.5 Hz, 4-CH), 3.73 (3H, s, OCH_3), 3.76 (3H, s, OCH_3), 3.80 (3H, s, OCH_3), 4.71 (1H, m, 3'-CH), 4.86 (1H, qua, J = 6.0 Hz, 5'-CH), 5.45 (1H, s, 4'-CH), 5.55 (1H, d, J = 1.74 Hz, 1'-CH), 6.01 (1H, s, 1-CH), 6.49 (1H,

d, J = 6.8 Hz, $NHCOCF_3$), 6.24 (1H, d, J = 10.2 Hz, ArH), 6.82 (1H, d, J = 10.2 Hz, ArH), 8.29 (4H, s, PNB).

Step 3: (1'S, 1R, 3S)-1-(4'-p-nitrobenzoyl-3'-trifluoroacetamido-2',3',6'-trideoxy-lyxohexopyranose)-3-methoxycarbonyl-3-methyl-5,8-dioxo-4,5,8-trihydro-1H-benzo-[2,3-c]-pyran

The titled compound was obtained via CAN oxidation (step 3, example 13) of the (1'S,1R,3S) precursor from step 2 herein.

^1H NMR ($CDCl_3$ 250 MHz, Bruker): δ, 1.30 (3H, d, J = 6.5 Hz, 6'-CH_3), 1.57 (3H, s, 3-CCH_3), 1.93-2.05 (2H, m, 2'-CH_2), 2.36 (1H, d, J = 20 Hz, 4-CH), 3.31 (1H, d, J = 20 Hz, 4-CH), 3.67 (3H, s, OCH_3), 4.46 (1H, m, 3'-CH), 4.66 (1H, qua, J = 6.5 Hz, 5'-CH), 5.36 (1H, s, 4'-CH), 5.62 (1H, s, 1'-CH), 5.93 (1H, s, 1-CH), 6.56 (1H, d, J = 7.1 Hz, $NHCOCF_3$), 6.77 (1H, d, J = 9.7 Hz, Quin-H). 6.85 (1H, d, J = 9.7 Hz, Quin-H), 8.30 (4H, m, PNB).

IR (Nicolet, 205 FT, film on NaCl plate): cm^{-1}, 3347.1, 2924.7, 2851.4, 1736.3, 1663.1, 1527.9, 1351.4, 1272.6, 1167.4, 951.60, 837.00, 718.80.

Step 4: (1'S, 1R, 3S)-1-(4'-p-nitrobenzoyl-3'-trifluoroacetamido-2',3',6'-trideoxy-lyxohexopyranose)-3-methoxy-carbonyl-3-methyl-5,10-dioxo-4,5,10-trihydro-1H-naphtho-[2,3-c]-pyran

The titled compound was obtained following cycloaddition between 1-acetoxybutadiene and the precursor from step 3 herein as per previously described procedure.

^1H NMR ($CDCl_3$ 250 MHz, Bruker): δ, 1.34 (3H, d, J = 6.5 Hz, 6'-CH_3), 1.59 (3H, s, 3-CCH_3), 1.90-2.10 (2H, m, 2'-CH_2), 2.50 (1H, d, J = 19.4 Hz, 4-CH), 3.49 (1H, d, J = 19.4 Hz, 4-CH), 3.65 (3H, s, OCH_3), 4.46 (1H, m, 3'-CH), 4.79 (1H, qua, J = 6.5 Hz, 5'-CH), 5.40 (1H, br s, 4'-CH), 5.65 (1H, d, J = 2.5 Hz, 1'-CH), 6.10 (1H, s, 1-CH), 6.51 (1H, d, J = 7.6 Hz, $NHCOCF_3$), 7.76 (2H, m, 7, 8-ArH), 8.13 (2H, m, 6, 9-ArH), 8.31 (4H, m, PNB).

IR (Nicolet, 205 FT, film on NaCl plate): cm^{-1}, 3333.8, 2919.5, 2851.0, 1739.0, 1667.4, 1533.4, 1790.5, 1271.8, 1212.6, 1187.7, 1103.6, 994.58, 949.75, 723.70.

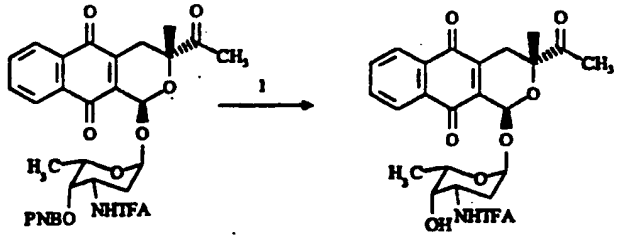
Step 5: **(1'S, 1R, 3S)-1-(3'-trifluoroacetamido-2',3',6'-trideoxy-L-lyxohexopyranose)-5,10-dioxo-4,5,10-trihydro-1H-naphtho-[2,3-c]-pyran (BCH-2077)**

The titled compound was obtained following methanolysis of the precursor from step 4.

^{1}H NMR ($CDCl_3$, 250 MHz, Bruker): δ, 1.39 (3H, d, J = 6.0 Hz, 6'-CH_3), 1.58 (3H, s, 3-CCH_3), 1.77 (1H, dd, J = 12.0 Hz, 4.1 Hz, 2'-HCH_a), 1.84 (1H, dd, J = 12.1 Hz, 5.9 Hz, 2'-HCH_a), 1.96 (1H, d, J = 8.7 Hz, 4'-OH), 2.48 (1H, d, J = 19.5 Hz, 4-HCH_a), 3.47 (1H, d, J = 19.5 Hz, 4-HCH_e), 3.60 (1H, d, J = 8.7 Hz, 4'-CH), 3.64 (3H, s, OCH_3), 4.17 (1H, m, 3'-CH), 3.56 (1H, qua, J = 6.0 Hz, 5'-CH), 5.46 (1H, d, J = 2.9 Hz, 1'-CH), 6.05 (1H, s, 1-CH), 6.71 (1H, d, J = 8.8 Hz, $NHCOCF_3$), 7.75 (2H, m, 7, 8-ArH), 8.10 (2H, m, 6, 9-ArH).

IR (Nicolet , 205 FT, film on NaCl plate): cm^{-1}, 3420.6, 2934.5, 1735, 1721.8, 1665.8, 1291.8, 1182.3, 1166.3, 1112.9, 776.7, 944.6, 912.6, 728.97.

Example 54: **Preparation of (1'S,1S,3R)-1-(3'-trifluoroacetamido-2',3',6'-trideoxy-lyxo-L-hexopyranose)-3-acetyl-3-methyl-3,4,5,10-tetrahydro-5,10-dioxo-naphtho-[2,3-c] pyran (BCH-2082)**



BCH-2082

Step 1: **(1'S, 1S, 3R)-1-(3'-trifluoroacetamido-2',3',6'-trideoxy-L-lyxohexopyranose)-3-acetyl-3-methyl-5,10-dioxo-4,5,10-trihydro-1H-naphtho-[2,3-c]-pyran (BCH-2082)**

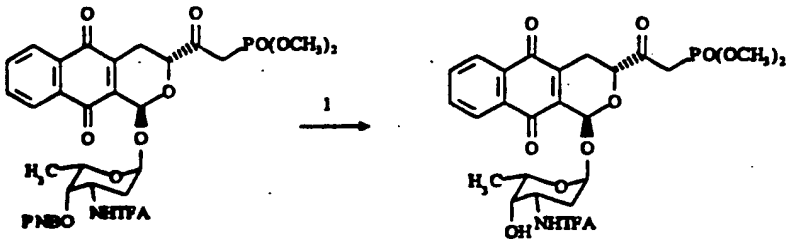
Methanolysis of the p-nitrobenzoylated precursor yielded the titled product.

^{1}H NMR ($CDCl_3$, 250 MHz, Bruker): δ, 1.31 (1H, d, J = 6.6 Hz, 6'-CH_3), 1.45 (3H, s, 3-CCH_3), 1.80 (1H, d, J = 8.8 Hz, 2'-CH), 1.81 (1H, d, J =

10 Hz, 2'-CH), 2.24 (3H, s, $COCH_3$), 2.52 (1H, d, J = 18.5 Hz, 4-HCH_a), 3.38 (1H, d, J = 18.5 Hz, 4-HCH_e), 3.60 (1H, br s, 4'-CH), 4.19 (1H, br qua, J = 10 Hz, 3'-CH), 4.41 (1H, qua, J = 6.6 Hz, 5'-CH), 5.45 (1H, s, 1'-CH), 6.13 (1H, s, 1-CH), 6.63 (1H, d, J = 10 Hz), 7.75 (2H, m, 7, 8-ArH), 8.09 (2H, m, 6, 9-ArH).

IR (Nicolet , 205 FT, film on NaCl plate): cm^{-1}, 3375.1 (br str), 3091.1, 2929.6, 1715.2, 1671.2, 1597.7, 1293.3, 1172.9, 981.5, 729.22.

Example 55: Preparation of (1'S,1S,3R)-1-(3'-trifluoroacetamido-2',3',6'-trideoxy-lyxo-L-hexopyranose)-3-dimethoxyphosphonoacetyl-3,4,5,10-tetrahydro-5,10-dioxo-naphtho-[2,3-c] pyran (BCH-1690)



BCH-1690

Step 1: (1'S,1S,3R)-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3-dimethylphosphonoacetyl-5,10-dioxo-3,4,5-10-tetrahydro-1H-naphtho-[2,3-c]-pyran (BCH-1690)

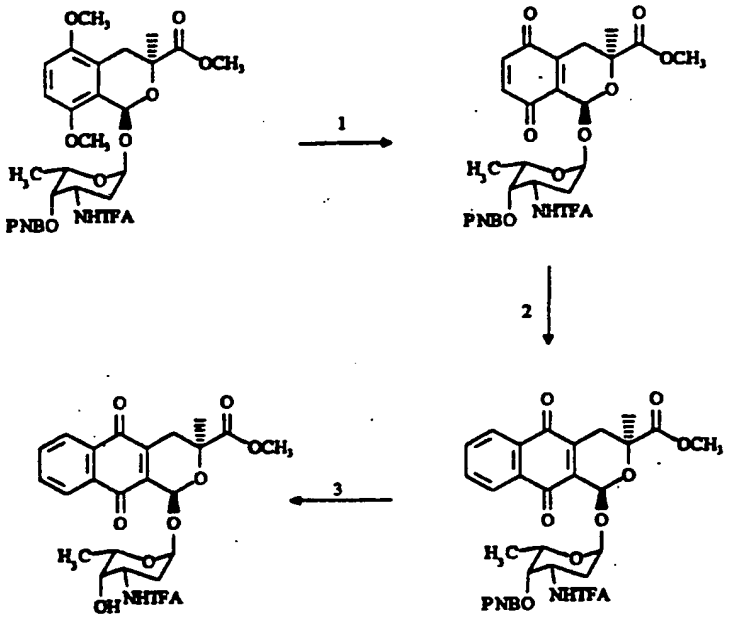
The p-nitrobensoyl precursor was hydrolyzed with catalytic sodium methoxide in methanol as per previously described procedure. The titled compound had:

M.P. 91-93°C,

^1H NMR ($CDCl_3$, 250 MHz, Bruker): δ, 1.40 (3H, d, J = 7.6 Hz, 6'-CH_3), 1.89 (2H, m, 2'-CH_2), 2.62 (1H, dd, J = 18.2 Hz, 11.8 Hz, 4-HCH_a), 3.00 (1H, dd, J = 18.2 Hz, 4.1 Hz, 4-HCH_e), 3.65 (1H, br s, 4-CH), 3.83 (3H, s, $POCH_3$), 3.87 (3H, s, $POCH_3$), 4.32 (1H, qua, J = 7.6 Hz, 5'-CH), 4.56 (1H, m, 3-CH), 4.99 (1H, br s CHP), 5.13 (1H, br s, CHP), 5.44 (1H, s, 1'-CH), 6.09 (1H, s, 1-CH), 6.83 (1H, br d, J = 7.6 Hz, $NHCOCF_3$), 7.77 (2H, m, 7, 8-ArH), 8.09 (2H, m, 6, 9-ArH).

IR (Nicolet 205 FT, film on NaCl plate): cm^{-1}, 3421.9, 2958.3, 1716.0, 1665.6, 1592.5, 1287.6, 1181.8, 1045.7, 977.7, 858.4, 727.5.

Example 56: **Preparation of (1'S,1S,3S)-1-(3'-trifluoroacetamido-2',3',6'-trideoxy-lyxo-L-hexopyranose)-3-methoxycarbonyl-3-methyl-3,4,5,10-tetrahydro-5,10-dioxo-naphtho-[2,3-c] pyran (BCH-2081)**



Step 1: **(1'S, 1S, 3S)-1-(4'-p-nitrobenzoyl-3'-trifluoroacetamido-2',3',6'-trideoxy-lyxohexopyranose)-3-methoxy-carbonyl-3-methyl-5,8-dioxo-4,5,8-trihydro-1H-benzo-[2,3-c]-pyran.**

CAN oxidation of the (1'S,1R,3S) precursor from step 2, example 53, yielded the titled compound.

^{1}H NMR ($CDCl_3$ 250 MHz, Bruker): δ, 1.14 (3H, d, J = 6.0 Hz, 6'-CH_3), 1.61 (3H, s, 3-CCH_3), 1.96 (1H, d tr, J = 11.7 Hz, 4.1 Hz, 2'-CH), 2.10 (1H, dd, J = 11.7 Hz, 2.9 Hz, 2'-CH), 2.58 (1H, d, J = 18.2 Hz, 4-CH), 3.00 (1H, d, J = 18.2 Hz, 4-CH), 3.71 (3H, s, OCH_3) 4.50 (1H, qua, J = 6.0 Hz, 5'-CH), 4.60 (1H, m, 3'-CH), 5.42 (1H, s, 4'-CH), 5.56 (1H, s, 1'-CH), 6.03 (1H, s, 1-CH), 6.58 (1H, d, J = 7.4 Hz, $NHCOCF_3$), 6.72 (1H, d, J = 8.8 Hz, Quin-H), 6.78 (1H, d, J = 8.8 Hz, Quin-H), 8.24 (4H, br s, PNB).

IR (Nicolet, 205 FT, film on NaCl plate): cm^{-1}, 3340.0, 3084.6, 2950.7, 2857.2, 1732.8, 1664.3, 1533.4, 1349.7, 1268.7, 1159.7, 1013.3, 955.70, 837.03, 735.00.

Step 2: (1'S, 1S, 3S)-1-(4'-p-nitrobenzoyl-3'-trifluoroacetamido-2',3',6'-trideoxy-lyxohexopyranose)-3-methoxy-carbonyl-3-methyl-5,10-dioxo-4,5,10-trihydro-1H-naphtho-[2,3-c]-pyran

The titled compound was obtained following cycloaddition between 1-acetoxybutadiene and the quinone from step 1 herein.

^{1}H NMR ($CDCl_3$ 250 MHz, Bruker): δ, 1.16 (3H, d, J = 6.0 Hz, 6'-CH_3), 1.67 (3H, s, 3-CCH_3), 2.05 (2H, m, 2'-CH_2), 2.77 (1H, dd, J = 17.6 Hz, 0.6 Hz, 4-HCH_a), 3.22 (1H, dd, J = 17.6 Hz, 1.8 Hz, 4-HCH_e), 3.73 (3H, s, OCH_3), 4.57 (1H, qua, J = 6.0 Hz, 5'-CH), 4.64 (1H, m, 3'-CH), 5.45 (1H, d, J = 2.1 Hz, 4'-CH), 5.67 (1H, s, 1'-CH), 6.22 (1H, s, 1-CH), 6.34 (1H, d, J = 8.2 Hz, $NHCOCF_3$), 7.76 (2H, m, 7, 8-ArH), 8.08 (2H, m, 6, 9-ArH), 8.28 (4H, m, PNB).

IR (Nicolet, 205 FT, film on NaCl plate): cm^{-1}, 3331.7, 2957.1, 1734.1, 1708.5, 1666.4, 1595.6, 1527.9, 1271.3, 1216.2, 1181.61, 1165.8, 1104.5, 1013.2, 954.94, 731.40, 721.98.

Step 3: (1'S, 1S, 3S)-1-(3'-trifluoroacetamido-2',3',6'-trideoxy-lyxohexopyranose)-3-methoxycarbonyl-3-methyl-5,10-dioxo-4,5,10-trihydro-1H-naphtho-[2,3-c]-pyran (BCH-2081)

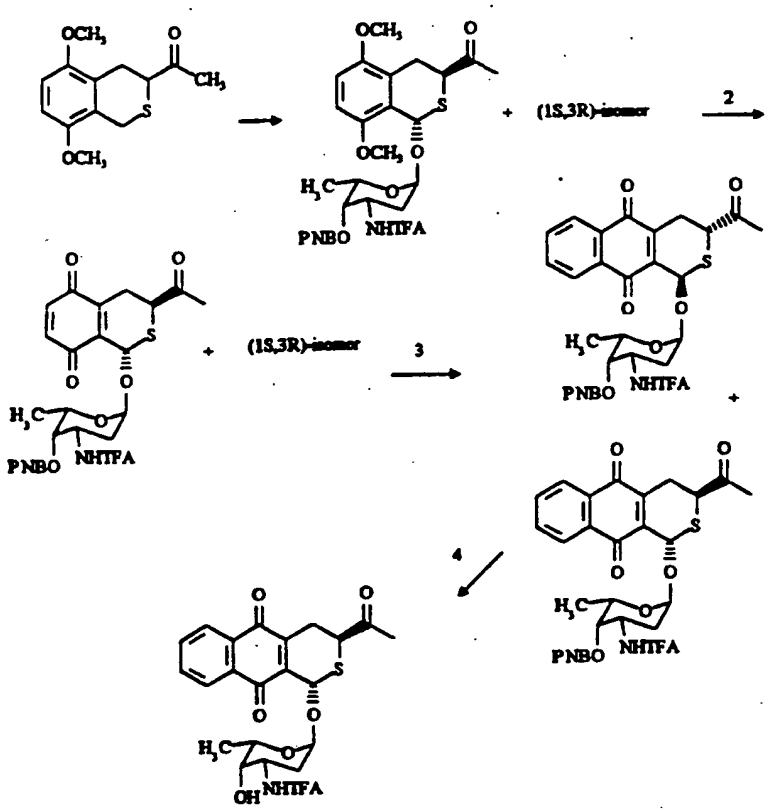
The precursor from step 2 herein was hydrolyzed with sodium methoxide (catalytic) as per previously described procedure. The product had:

^{1}H NMR ($CDCl_3$ 250 MHz, Bruker): δ, 1.23 (3H, d, J = 6.1 Hz, 6'-CH_3), 1.64 (3H, s, 3-CH_3), 1.79 (1H, d tr, J = 12.9 Hz, 3.8 Hz, 2'-HCH_a), 1.88 (1H, dd, J = 13.0 Hz, 4.7 Hz, -2'-HCH_e), 1.94 (1H, d, J = 7.6 Hz, 2'-OH), 2.74 (1H, d, J = 18.8 Hz, 4-HCH_a), 3.17 (1H, d, J = 18.8 Hz, 4-HCH_e), 3.61 (1H, d, J = 7.8 Hz, 4'-CH), 3.71 (3H, s, OCH_3), 4.32 (1H, m, 3'-CH), 4.40 (1H, qua, J = 6.1 Hz, 5'-CH), 5.50 (1H, d, J = 3.5 Hz, 1'-CH), 6.15 (1H, s, 1-CH), 6.67 (1H, d, J = 8.8 Hz, $NHCOCF_3$), 7.74 (2H, m, 7, 8-ArH),8.07 (2H, m, 6,9-ArH).

IR (Nicolet, 205 FT, film on NaCl plate): cm^{-1}, 3422.1 (br str), 2928.1, 2853.9, 1720.3, 1668.9, 1594.7, 1292.0, 1183.5, 1166.4, 1009.3, 986.49, 728.24.

Example 57: Preparation of (1'S,1S,3S)-1-(3'-trifluoroacetamido-2',3',6'-trideoxy-lyxo-L-hexopyranose)-3-

dimethoxyphosphonoacetyl-3,4,5,10-tetrahydro-5,10-dioxo-naphtho-[2,3-c] thiopyran (BCH-2037.001)



Example 1

Step 1: Preparation of (1'S,1S,3S) and (1'S,1R,3R)-1-(3'-trifluoroacetamido-2',3',6'-trideoxy-L-lyxohexopyranose)-3-acetyl-5,8-dimethoxy-thioisochroman

The compound from step 1, example 13, and daunosamine precursor (259 mg, 0.66 mmole) were dissolved in CH_2Cl_2 (25 ml) and left stirring in presence of molecular sieve for 30 minutes before DDQ (150 mg, 0.66 mmole) was added. The resulting mixture was stirred for 2 1/2 hours. $NaHCO_3$ (5% solution) was added and the aqueous layer was extracted with CH_2Cl_2. The combined organic phases were washed with H_2O, dried over $MgSO_4$, filtered and concentrated in vacuo. The crude obtained was flash chromatographed using Tol:EE (9:1) to give a pure mixture of two titled isomers (in 60% yield) which was used to carry out the next step.

Step 2: **Preparation of (1'S,1S,3S) and (1'S,1R,3R)-1-(4'-p-nitrobenzoyl-3'-trifluoroacetamido-2',3',6'-trideoxy-L-lyxohexopyranose)-3-acetyl-5,8-dioxo-4,5,8-trihydro-1H-benzo-[2,3-c]-pyran**

The compound from step 1 herein (112.7 mg, 0.18 mmole) was dissolved in acetonitrile (5 ml), cooled to 0°C, followed by the addition of $NaHCO_3$ (29 mg, 0.34 mmole) and some H_2O. The resulting mixture was stirred for 5 minutes before CAN (296 mg, 0.54 mmole) was added. After all CAN was added, the reaction mixture was stirred 10 minutes extra 0°C, then warmed to room temperature. H_2O was added and it was extracted with CH_2Cl_2. The combined organic phases were washed with H_2O, dried over $MgSO_4$, filtered and concentrated in vacuo. The crude containing a mixture of two titled diastereoisomers was used in the following step.

Step 3: **(1'S,1S,3S)-1-(4'-p-nitrobenzoyl-3'-trifluoroacetamido-2',3',6'-trideoxy-L-lyxohexopyranose)-3-acetyl-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-thiopyran**

Following the example 1, step 1, a mixture of the two titled adducts was obtained which could be seperated via flash chromatography. The first eluent had:

^1H NMR (acetone-d_6, 250 MHz, Bruker): δ, 1.23 (3H, d, J = 5.6 Hz, 6'-CH_3), 1.70-1.90 (2H, m, 2'-CH_2), 2.44 (3H, s, $COCH_3$), 2.84 (1H, dd, J = 17.8 Hz, 11.8 Hz, 4-HCH_a), 3.36 (1H, dd, J = 17.8 Hz, 4.1 Hz, 4'-HCH_e), 4.53 (1H, dd, J = 11.8 Hz, 4.1 Hz, 3-CH), 4.60 (1H, m, 3'-CH), 4.75 (1H, qua, J = 5.6 Hz, 5'-CH), 5.53 (1H, s, 4'-CH), 5.70 (1H, d, J = 2.3 Hz, 1'-CH), 6.13 (1H, s, 1-CH), 7.90 (2H, m, 7, 8-ArH), 8.12 (2H, m, 6, 9-ArH), 8.39 (4H, m, PNB), 8.65 (1H, d, J = 5.8 Hz, $NHCOCF_3$).

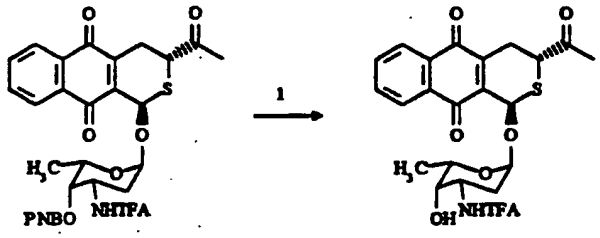
The second eluent had:

^1H NMR (acetone-d_6, 250 MHz, Bruker): δ, 1.32 (3H, d, J = 6.8 Hz, 6'-CH_3), 2.39 (3H, s, $COCH_3$), 1.94 (1H, dd, J = 12.3 Hz, 4.1 Hz, 2'-HCH_a), 2.50 (1H, tr d, J = 12.3 Hz, 2.9 Hz, 2'-HCH_e), 2.89 (1H, dd, J = 18.2 Hz, 11.2 Hz, 4-HCH_a), 3.35 (1H, dd, J = 18.2 Hz, 3.5 Hz, 4-HCH_e), 4.41 (1H, dd, J = 11.2 Hz, 3.5 Hz, 3-CH), 4.52 (1H, m, 3'-CH), 4.66 (1H, qua, J = 6.8 Hz, 5'-CH), 5.47 (1H, s, 4'-CH), 5.74 (1H, d, J = 2.9 Hz, 1'-CH), 6.31 (1H, s, 1-CH), 7.91 (2H, m, 7, 8-ArH), 8.14 (2H, m, 6, 9-ArH), 8.38 (4H, m, PNB), 8.68 (1H, d, J = 7.1 Hz, $NHCOCF_3$).

Step 4: (1'S,1S,3S)-1-(3'-trifluoroacetamido-2',3',6'-trideoxy-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-thiopyran (BCH-2037.001)

^{1}H NMR ($CDCl_3$ 250 MHz, Bruker): δ, 1.43 (3H, s, 6'-CH_3), 1.83-1.98 (2H, m, 2'-CH_2), 2.37 (3H, s, $COCH_3$), 2.90 (1H, dd, J = 17.8 Hz, 12 Hz, 4-HCH_a), 3.32 (1H, dd, J = 17.8 Hz, 4.1 Hz, 4-HCH_e), 3.61 (1H, br s, 4'-CH), 4.07 (1H, dd, J = 12.0 Hz, J = 4.1 Hz, 3-CH), 5.53 (1H, s, 1'-CH), 6.21 (1H, s, 1-CH), 6.74 (1H, d, J = 7.6 Hz, $NHCOCF_3$), 7.76 (2H, m, 7, 8-ArH), 8.12 (2H, m, 6, 9-ArH).

Example 58: Preparation of (1'S,1R,3R)-1-(3'trifluoroacetamido-2',3',6'-trideoxy-lyxo-L-hexopyranose)-3-dimethoxyphosphonoacetyl-3,4,5,10-tetrahydro-5,10-dioxo-naphtho-[2,3-c] pyran (BCH-2127)



BCH-2127

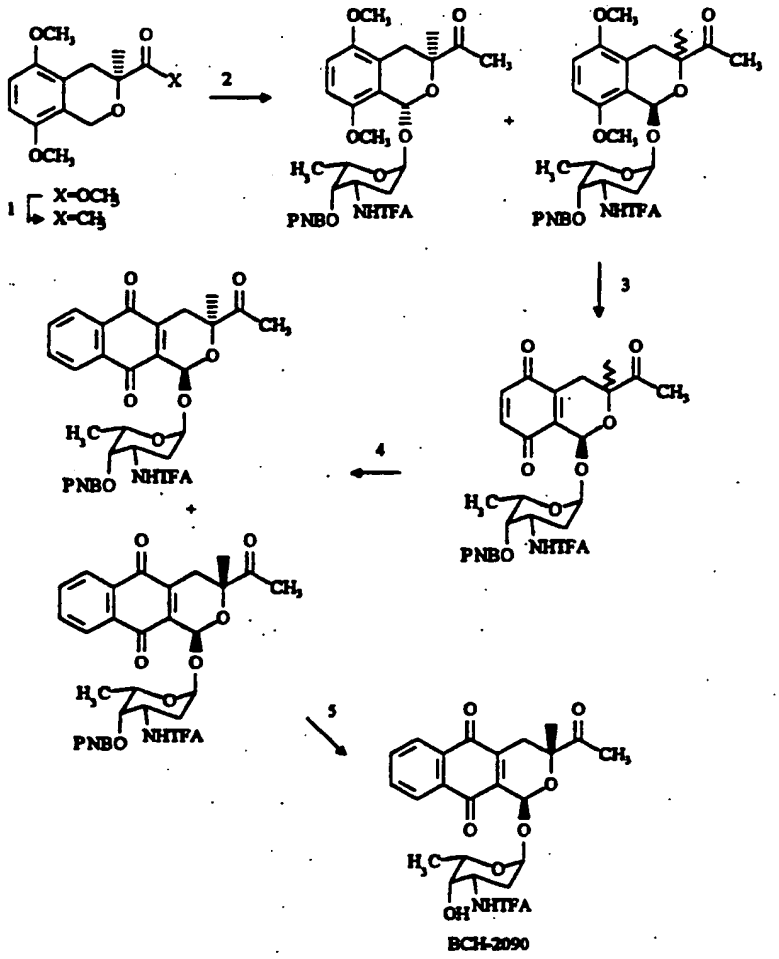
Step 1: (1'S, 1R, 3R)-1-(3'-trifluoroacetamido-2',3',6'-trideoxy-L-lyxohexopyranose)-3-acetyl-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-thiopyran (BCH-2127)

The second eluent from step 3, example 57, was hydrolyzed with catalytic sodium methoxide in methanol. The titled compound had:

^{1}H NMR ($CDCl_3$ 250 MHz, Bruker): δ, 1.43 (3H, d, J = 6.5 Hz, 6'-CH_3), 1.80-2.00 (2H, m, 2'-CH_2), 2.37 (3H, s, $COCH_3$), 2.91 (1H, dd, J = 18.3 Hz, 11.8 Hz, 4-HCH_a), 3.33 (1H, dd, J = 18.3 Hz, 4.7 Hz, 4-HCH_e), 3.60 (1H, br s, 4-CH), 4.07 (1H, dd, J = 11.8 Hz, 4.7 Hz, 3-CH), 4.25 (1H, m, 3'-CH), 4.35 (1H, qua, J = 6.5 Hz, 5'-CH), 5.53 (1H, d, J = 2.4 Hz, 1'-CH), 6.21 (1H, s, 1-CH), 6.74 (1H, d, J = 7.6 Hz, $NHCOCF_3$), 7.76 (1H, m, 7, 8-ArH), 8.14 (2H, m, 6, 9-ArH).

Example 59: Preparation of (1'S,1S,3S)-1-(3'-trifluoroacetamido-2',3',6'-trideoxy-lyxo-L-hexopyranose)-3-acetyl-3-

methyl-3,4,5,10-tetrahydro-5,10-dioxo-1H-naphtho-[2,3-c] pyran (BCH-2090)



Step 1: 3-acetyl-3-methyl-5,8-dimethoxy isochroman

The compound from step 1, example 53, (126.5 mg, 0.474 mmol) was dissolved in ether and then cooled to -78°C. Methyllithium (1.4 M in ether (0.71 ml, 0.995 mmol) was added. After 10 minutes methanol was added. The reaction mixture was acidified with HCl (0.5 N) and extracted with ethyl acetate. The organic layer was dried over sodium sulfate and then evaporated to give a crude product (121 mg). ^1H NMR showed that it was a mixture of starting material and product in 1:1 ratio. Chromatography allowed isolution of the desired titled product as a gel.

^1H NMR ($CDCl_3$ 250 MHz, Bruker): δ, 1.37 (3H, s, 3-CCH_3), 2.24 (3H, s, $COCH_3$), 2.59 (1H, d, J = 17.6 Hz, 4-CH), 2.99 (1H, d, J = 17.6 Hz, 4-

CH), 3.74 (3H, s, OCH_3), 3.76 (3H, s, OCH_3), 4.77 (2H, s, 1-CH_2), 6.57 (1H, d, J = 9.4 Hz, ArH), 6.62 (1H, d, J = 9.4 Hz, ArH).
IR (Nicolet, film on NaCl plate): cm^{-1}, 2941.9, 2834.4, 1721.6, 1482.4, 1340.2, 1257.0, 1061.4, 795.30, 716.80

Step 2: (1'S,1S,3S) and (1'S,1S,3R)-1-(4'-p-nitrobenzoyl-3'-trifluoroacetamido-2',3',6'-trideoxy-L-lyxohexopyranose)-3-acetyl-3-methyl-5,8-dimethoxy-isochroman

The compound from step 1 herein (67 mg, 0.268 mmol) was stirred with DDQ (91.3 mg, 0.422 mmol) and 4',5'-protected daunosamine (157 mg, 0.402 mmol) in methylene chloride at 40°C for 24 hours. The solvent was evaporated. The crude product was chromatographed (hex:EtOAc = 10:4) to give the titled compounds (88 mg containing two isomers in 2:1 ratio inseparable).
^1H NMR ($CDCl_3$ 250 MHz, Bruker): δ, 1.23 (3H, d, J = 6.0 Hz, A-6'-CH_3), 1.22 (3H, d, J = 6.0 Hz, B-6'-CH_3), 1.44 (3H, s, A-3-CCH_3), 1.66 (3H, s, B-3-CCH_3), 1.84 (1H, m, A-2'-CH), 1.84 (1H, m, A-2'-CH), 1.84 (1H, m, B-2'-CH), 2.14 (1H, m, A-2'-CH), 2.15 (1H, m, B-2'-CH), 2.80 (1H, d, J = 15.9 Hz, A-4-CH), 3.02 (2H, s, B-4-CH_2), 3.14 (1H, d, J = 15.9 Hz, A-4-CH), 3.77 (6H, s, B-OCH_3), 3.80 (6H, s, A-OCH_3), 4.41 (1H, qua, J = 6.0 Hz, B-5'-CH), 4.47 (1H, m, B-3'-CH), 4.56 (1H, qua, J = 6.0 Hz, A-5'-CH), 4.61 (1H, m, A-3'-CH), 5.40 (1H, s, B-4'-CH), 5.44 (1H, s, A-4'-CH), 5.61 (1H, d, J = 2.5 Hz, B-1'-CH), 5.70 (1H, d, J = 2.2 Hz, A-1'-CH), 6.35 (1H, s, B-1-CH), 6.37 (1H, s, A-1-CH), 6.41 (1H, d, J = 7.6 Hz, B-$NHCOCF_3$), 6.46 (1H, d, J = 7.8 Hz, A-$NHCOCF_3$), 6.76 (2H, m, B-ArH), 6.81 (2H, m, A-ArH), 8.25 (8H, br s, A-PNB, B-PNB).
IR (Nicolet, 205 FT, film on NaCl plate): cm^{-1}, 3327.9, 2945.2, 2840.3, 1732.6, 1528.4, 1489.4, 1351.8, 1263.4, 1167.8, 1116.3, 1105.2, 969.06, 948.80, 801.62, 720.66.
Also obtained from this reaction (34 mg) was (1'S, 1R, 3S)-1-(4'-p-nitrobenzoyl-3'-trifluoroacetamido-2',3',6'-trideoxylyxohexopyranose)-3-acetyl-3-methyl-5,8-dimethoxy-isochroman which had:
^1H NMR ($CDCl_3$ 250 MHz, Bruker): δ, 1.18 (3H, d, J = 7.6 Hz, 6'-CH_3), 1.51 (3H, s, 3-CCH_3), 2.00-2.10 (2H, m, 2'-CH_2), 2.84 (1H, d, J = 17.1 Hz, 4-CH), 2.96 (1H, d, J = 17.1 Hz, 4-CH), 3.77 (3H, s, OCH_3), 3.78 (3H, s, OCH_3), 4.54 (1H, qua, J = 7.6 Hz, 5'-CH), 4.62 (1H, m, 3'-CH), 5.46 (1H, d, J = 2.1 Hz, 4'-CH), 5.56 (1H, s, 1'-CH), 6.14 (1H, s,

1-CH), 6.41 (1H, d, J = 7.6 Hz, $NHCOCF_3$), 6.70 (1H, d, J = 8.8 Hz, ArH), 6.76 (1H, d, J = 8.8 Hz, ArH), 8.26 (4H, m, PNB).
IR (Nicolet, 205 FT, film on NaCl plate): cm^{-1}, 3336.5, 2940.0, 2834.3, 1730.3, 1527.2, 1481.4, 1266.3, 1163.6, 975.8, 718.02.

Step 3: (1'S,1S,3S) and (1'S, 1S, 3R)-1-(4'-p-nitrobenzoyl-3'-trifluoroacetamido-2',3',6'-trideoxy-lyxohexopyranose)-3-acetyl-3-methyl-5,8-dioxo-4,5,8-trihydro-1H-benzo-[2,3-c]-pyran

CAN oxidation of the products from step 2 herein gave the titled quinones (as per procedure step 2, example 14).
^1H NMR ($CDCl_3$ 250 MHz, Bruker): δ, 1.30 (3H, d, J = 6.0 Hz, A-6'-CH_3), 1.27 (3H, d, J = 6.1 Hz, B-6'-CH_3), 1.44 (3H, s, A-3-CCH_3), 1.44 (3H, s, B-3-CCH_3), 1.80-2.30 (4H, m, A-2'-CH_2, B-2'-CH_2), 2.62 (1H, d, J = 18.1 Hz, A-4-HCH_a), 2.72 (1H, d, J = 18.1 Hz, A-4-HCH_e), 2.70 (1H, d, J = 18.0 Hz, B-4-CH), 3.25 (1H, d, J = 18 Hz, B-4'-CH), 4.41 (1H, m, B-3'-CH), 4.56 (1H, m, A-3'-CH), 4.57 (1H, qua, J = 6 Hz, B-5'-CH), 4.72 (1H, qua, J = 6 Hz, A-5'-CH), 5.38 (1H, s, B-4'-CH), 5.42 (1H, s, A-4'-CH), 5.58 (1H, d, J = 2.4 Hz, B-1'-CH), 5.66 (1H, d, J = 2.9 Hz, A-1'-CH), 5.98 (1H, s, B-1-CH), 6.02 (1H, s, A-1-CH), 6.45 (1H, d, J = 8.1 Hz, B-$NHCOCF_3$), 6.55 (1H, d, J = 8 Hz, A-$NHCOCF_3$), 6.70-6.87 (4H, m, A-6, 7-Quin, B-6, 7-Quin), 8.28 (8H, m, A-PNB, B-PNB).
IR (Nicolet, 205 FT, film on NaCl plate): cm^{-1}, 3327.5, 3084.6, 2984.9, 2938.2, 1723.4, 1661.1, 1533.4, 1352.8, 1278.0, 1215.7, 1169.0, 1122.3, 948.30, 730.86.

Step 4: (1'S,1S,3S) and (1'S, 1S, 3R)-1-(4'-p-nitrobenzoyl-3'-trifluoroacetamido-2',3',6'-trideoxy-lyxohexopyranose)-3-acetyl-3-methyl-5,10-dioxo-4,5,10-trihydro-1H-naphtho-[2,3-c]-pyran

The quinone from step 3 herein was cycloadded with 1-acetoxybutadiene as per procedure described in step 3, example 14. The (1'S,1S,3R) titled compound had:
^1H NMR ($CDCl_3$ 250 MHz, Bruker): δ, 1.35 (3H, d, J = 5.9 Hz, 6'-CH_3), 1.49 (3H, s, 3-CCH_3), 1.95 (1H, dd, J = 12.6 Hz, 4.7 Hz, 2'-CH), 2.12 (1H, d tr, J = 12.6 Hz, 2.9 Hz, 2'-CH), 2.71 (1H, d, J = 18.2 Hz, 4-CH), 2.89 (1H, d, J = 18.2 Hz, 4-CH), 4.60 (1H, m, 3'-CH), 4.85 (1H, qua, J =

5.9 Hz, 5'-CH), 5.47 (1H, br s, 4'-CH), 5.71 (1H, d, J = 2 Hz, 1'-CH), 6.21 (1H, d, J = 1.2 Hz, 1-CH), 6.42 (1H, d, J = 7.6 Hz, $NHCOCF_3$), 7.78 (2H, m, 7, 8-ArH), 8.14 (2H, m, 6, 9-ArH), 8.31 (4H, m, PNB).

IR (Nicolet, 205 FT, film on NaCl plate): cm^{-1}, 3336.3, 2922.6, 2852.6, 1728.0, 1666.8, 1532.8, 1346.3, 1273.5, 1212.3, 1165.6, 1119.0, 1098.6, 996.7, 952.96, 836.3, 722.58.

The (1'S,1S,3S) diastereomer had:

^1H NMR ($CDCl_3$ 250 MHz, Bruker): δ, 1.31 (3H, d, J = 5.9 Hz, 6'-CH_3), 1.47 (3H, s, 3-CCH_3), 1.89 (1H, dd, J = 11.8 Hz, 5.3 Hz, 2'-HCH_a), 2.06 (1H, d tr, J = 11.8 Hz, 4.1 Hz, 2'-HCH_e), 2.55 (1H, d, J = 17.8 Hz, 4-HCH_a), 3.40 (1H, d, J = 17.8 Hz, 4-HCH_e), 4.45 (1H, m, 3'-CH), 4.66 (1H, qua, J = 5.9 Hz, 5'-CH), 5.43 (1H, s, 4'-CH), 5.63 (1H, d, J = 2.3 Hz, 1'-CH), 6.17 (1H, s, 1-CH), 6.30 (1H, d, J = 11.8 Hz, $NHCOCF_3$), 7.77 (2H, m, 7, 8-ArH), 8.13 (2H, m, 6, 9-ArH), 3.30 (4H, m, PNB).

Step 5: (1'S, 1S, 3S)-1-(3'-trifluoroacetamido-2',3',6'-trideoxy-L-lyxohexopyranose)-3-acetyl-3-methyl-5,10-dioxo-4,5,10-trihydro-1H-naphtho-[2,3-c]-pyran (BCH-2090)

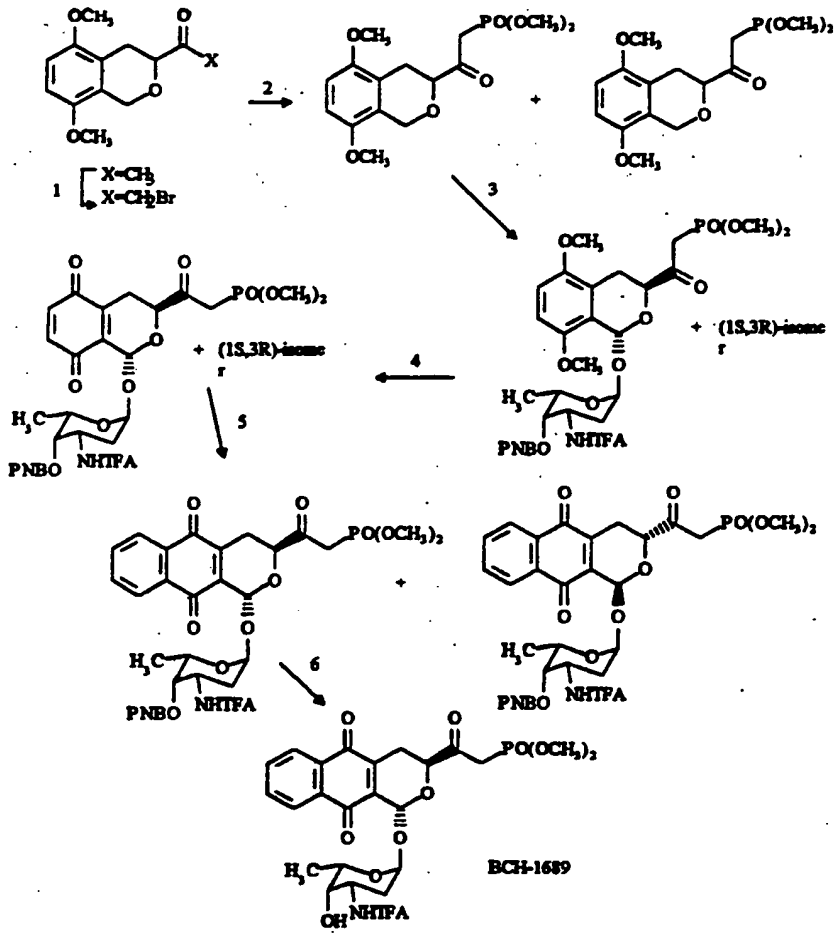
Hydrolysis of the (1'S,1S,3S) precursor from step 4 herein gave the titled compound.

M.P. 95°C.

^1H NMR ($CDCl_3$, 250 MHz, Bruker): δ, 1.41 (3H, d, J = 5.9 Hz, 6'-CH_3), 1.46 (3H, s, 3-CCH_3), 1.85 (2H, m, 2'-CH_2), 2.27 (3H, s, $COCH_3$), 2.84 (2H, d, J = 5.9 Hz, 4-CH_2), 3.65 (1H, s, 4'-CH), 4.31 (1H, m, 3'-CH), 4.64 (1H, qua, J = 6.0 Hz, 5'-CH), 5.53 (1H, br s, 1'-CH), 6.15 (1H, s, 1-CH),-6.71 (1H, br d, J = 8.8 Hz, $NHCOCF_3$), 7.75 (2H, m, 7, 8-ArH), 8.11 (2H, m, 6, 9-ArH).

IR (Nicolet , 205 FT, film on NaCl plate): cm^{-1}, 3423.2, 3342.2, 3087.5, 2987.2, 2933.2, 1717.6, 1667.5, 1590.3, 1289.3, 1216.0, 1179.1, 1167.6, 1124.2, 980.89, 940.05, 918.55, 734.22.

Example 60: Preparation of (1'S,1R,3S)-1-(3'-trifluoroacetamido-2',3',6'-trideoxy-lyxo-L-hexopyranose)-3-dimethoxyphosphonoacetyl-3,4,5,10-tetrahydro-5,10-dioxo-naphtho-[2,3-c] pyran (BCH-1689)



Step 1: 3-bromoacetyl-5,8-dimethoxy-isochroman

The titled compound was prepared by using 5,8-dimethoxy-3-acetoisochroman and the procedure from step 1, example 8.
^{1}H NMR ($CDCl_3$, 250 MHz, Bruker): 2.59 (1H, dd, J = 15.9 Hz, 11.8 Hz, 4-HCH_a), 3.03 (1H, dd, J = 15.9 Hz, 2.9 Hz, 4-HCH_e), 3.74 (3H, s, OCH_3), 3.75 (3H, s, OCH_3), 4.23 (1H, dd, J = 11.8 Hz, 2.9 Hz), 4.27 (1H, d, J = 13.5 Hz, CHBr), 4.34 (1H, d, J = 13.5 Hz, CHBr), 4.63 (1H, d, J = 15.9 Hz, 1-HCH_a), 4.96 (1H, d, J = 15.9 Hz, 1-HCH_e), 6.63 (2H, m, ArH).

Step 2: 3-dimethoxy phosphinoacetyl-5,8-dimethoxy-isochroman

The titled compound was obtained following treatment of the product from step 1 herein with $P(OCH_3)_3$.
^{1}HNMR ($CDCl_3$, 250 MHz, Bruker), δ:2.57 (dd, 1 H, J = 16.9 Hz, 11 Hz, 4 - HCH_a), 2.98 (dd, 1 H, J = 16.9 Hz, 2.9 Hz, 4 - HCH_e), 3.26 (dd, 1 H, J = 21.5 Hz, 14.5 Hz, COCHP), 3.54 (dd, 1 H, J = 21.5 Hz, 14.5 Hz, COCHP),

3.71 (s, 3 H, $ArOCH_3$), 3.72 (s, 3 H, $ArOCH_3$), 3.74 (d, 3 H, J = 4.3 Hz, $POCH_3$), 3.78 (d, 3 H, J = 4.3 Hz, $POCH_3$), 4.11 (dd, 1 H, J = 11 Hz, 3.4 Hz, 3 - CH), 4.63 (d, 1 H, J = 16.3 Hz, 1 HCH_a), 4.97 (d, 1 H, J = 16.3 Hz, 1 - HCH_e), 6.60 (m, 2 H, 6.7 - ArH).

IR (Nicolet, 205FT, film on NaCl plate), cm^{-1}: 2954.3, 2836.7, 1725.5 (str), 1603.9 (W), 1482.2, 1259.2 (str), 1034.7, 799.10, 715.8.

Step 3: (1'S,1S,3R) (1'S,1R,3S)-5,8-dimethoxyl(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-p-nitrobenzoyl-L-lyxohexopyranose)-3-dimethylphosphonoacetyl isochroman

To a stirred solution of the phosphonate from step 2 herein (199 mg, 0.58 mmole) with 4 - PNB - 3 - TFA - daunosamine (270 mg, 0.69 mmole) in clichloromethane (60 ml) was added 4 pelets of molecular sieves (4A°). This was followed by addition of dichlorodisyanoquinone (DDQ, 170 mg, 0.75 mmole) in one portion. The resulting green liquid was stirred at 40 °C (controlled by an Ikamag-Ret-G-Heating-Stirring system) in a enclosed system for 25 hours then at room temperature (without heating) for 48 hours. The resulting muddy mixture was evaporated and then directly chromatographed (Hex:EA = 1:1.5) to yield the desired titled glycosides (diastereomeric mixture A and B, as light-colored glassy material, 407 mg).

^{1}HNMR ($CDCl_3$, 250 MHz, Bruker), δ:1.20 (d, 3 H, J = 7.0 Hz, 6' - CH_{3A}), 1.23 (d, 3 H, J = 7.0 Hz 6' - CH_{3B}), 1.82 (dd, 1 H, J = 12.2 Hz, 4.5 Hz, 2' - HCH_{Aa}), 1.91 (dd, 1 H, J = 12.3 Hδ, 4.6 Hz, 2' - HCH_{Ba}), 2.07 (dt, 1 H, J = 12.3 Hz, 3.5 Hz, 2' - HCH_{Ae}), 2.20 (dt, 1 H, J = 12.4 Hz, 4 Hz, 2' - HCH_{Be}), 2.54 (dd, 1 H, J = 16.9 Hz, 13.4 Hz, 4 - HCH_{Ba}), 2.60 (dd, 1 H, J = 17 Hz, 11 Hz, 4 - HCH_{Aa}), 2.96 (dd, 1 H, J = 11 Hz, 3.5 Hz, 4 - HCH_{Ae}), 3.03 (dd, 1 H, J = 11.1 Hz, 3.3 Hz, 4 - HCH_{Be}), 3.74 - 3.87 (8xs, 24 H, 2 x $ArOCH_{3A}$, 2 x $ArOCH_{3B}$, 2 x $POCH_{3A}$, 2 x $POCH_{3B}$), 4.41 (qua, 1 H, J = 6.0 Hz, 5' - CH_B), 4.50 - 4.68 (M, 4 H, 3' - CH_A, 3' - CH_B, 3 - CH_A, 3 - CH_B), 4.70 (qua, 1 H, J = 7.0 Hz, 5' - CH_A), 4.99 (d, 2 H, J = 16 Hz, $COCH_{2A}P$), 5.03 (d, 2 H, J = 16.7 Hz, $CoCH_{2B}P$), 5.41 (s, 1 H, 4' - CH_B), 5.47 (s, 1 H, 4' - CH_A), 5.57 (s, 1 H, 1' - CH_B), 5.61 (s, 1 H, 1' - CH_A), 5.98 (s, 1 H, 1 - CH_B), 6.15 (s, 1 H, 1 - CH_A), 6.71 (qua, 2 H, J = 8.7 Hz, 6.7 - ArH_B), 6.75 (qua, 2 H, J = 8.5 Hz, 6.7 - ArH_A), 6.89 (d, 1 H, J = 7.0 Hz, NH_BCOCF_3), 7.05 (d, 1 H, J = 7.0 Hz, NH_ACOCF_3), 8.21 (m, 8 H, 4 x $COArH_ANO_2$, 4 x $COArH_BNO_2$).

Step 4: [(1'S,1S,3R) and (1'S,1R,3S)-1-(2',3,6'-trideoxy-3'-trifluoroacetamido-4'-p-nitrobensoyl-L-lyxohexopyranose)-3-dimethylphosphonoacethyl-3,4,5,8-tetrahydronaphthaleno-[2,3-c]-pyran

To a solution of glycoside from step 3 herein (98 mg, 0.13 mmole) in 8 ml of acetonitrile cooled to 0°C was added sodium bicarbonate powder (22 mg, 0.27 mmole). This was followed by dropwise addition of aqueous cerium ammonium nitrate (CAN, 298 mg, 0.54 mmole in 3.0 ml of water). After 10 minutes at 0°C, the reaction mixture was poured to water (20 ml) and extracted with dichloromethane (4 x 10 ml). The organic layer was dried (over sodium sulfate) and evaporated to give the titled quinones as a glassy mixture (85 mg).

^{1}HNMR ($CDCl_3$, 250 MHz, Bruker), δ:1.15 (d, 1 H, J = 6.4 Hz, 6' - CH_{3B}), 1.30 (d, 1 H, J = 6.4 Hz 6' - CH_{3A}), 2.44-1.80 (M, 4 H, 2 - HCH_{Aa}, 2 - HCH_{Ba}, 2 - HCH_{Ae}, 2 - HCH_{Be}), 2.41 (dd, 1 H, J = 16.6 Hz, 11.6 Hz, 4 - HCH_{Ba}), 2.48 (dd, 1 H, J - 16.6 Hz, 11.3 Hz, 4 - HCH_{Aa}), 2.83 (dd, 1 H, J = 17.0 Hz, 5.23 Hz, 4 - HCH_{Ae}), 2.85 (dd, 1 H, J = 16.8 Hz, 5.0 Hz, 4 - HCH_{Be}), 3.79 (s, 3 H, $POCH_{3A}$), 3.84 (s, 3 H, $POCH_{3A}$), 3.82 (d, 3 H, J = 2.1 Hz, $POCH_{3B}$), 3.87 (d, 3 H, J = 2.1 Hz, $POCH_{3B}$), 4.34 (qua, 1 H, J = 7.0 Hz, 5' CH_B), 4.48 - 4.60 (m, 4 H, 3 - CH_A, 3 CH_B, 3' - CH_A, 3' - CH_B), 4.64 (qua, 1 H, J = 7.0 Hz, 5' - CH_A), 5.04 (d, 2 H, J = 25 Hz, $COCH_{2A}P$), 5.05 (d, 2 H, J = 31 Hz, $COCH_{2B}P$), 5.43 (s, 2 H, 4', CH_A, 4' - CH_B), 5.55 (s, 1 H, 1'- CH_A), 5.61 (s, 1 H, 1' - CH_B), 5.81 (s, 1 H , 1 - CH_B), 5.97 (s, 1 H, 1 - CH_A), 6.79 (m, 2 H, 6.7 - ArH_B), 6.82 (m, 2 H, 6.7 - ArH_A), 8.27 (s, 8 H, 4 x $COArH_ANO_2$, 4 x $COArH_BNO_2$).

Step 5: (1'S,1R,3S)-1-(2',3',6'-trideoxy-4'-p-niprobensoyl-3'-trifluoroacetamido-L-lyxohexo pyranose)-3-dimethyl phosphonoacetyl-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho[2,3-c]-pyran

The compounds from step 4 herein (85 mg, 0.121 mmol) were heated with 1-acetoxy-1,3-butadiene (86 µl, 0.723 mmol) in toluene at 45°C for 28 hours. Solvent was evaporated and the crude product was chromatographed three times (toluene:EtOAc: HOMe: acetone:HOAc = 240:75:10:10:1) to give the (1'S,1R,3S) isomer (21 mg) and the (1'S,1S,3R) isomer (18 mg). The titled compound had:

^1H NMR ($CDCl_3$, 250 MHz, Bruker): δ, 1.19 (3H, d, J = 7.0 Hz, 6'-CH_3), 2.03 (1H, m, 2-HCH_a), 2.07 (1H, m, 2-HCH_e), 2.56 (1H, dd, J = 18.2 Hz, 11.8 Hz, 4-HCH_a), 3.05 (1H, dd, J = 18.2 Hz, 4.7 Hz, 4-HCH_e), 3.85 (3H, d, J = 2.0 Hz, $POCH_3$), 3.91 (3H, d, J = 2.0 Hz, $POCH_3$), 4.40 (1H, qua, J = 7.0 Hz, 5'-CH), 4.60 (1H, m, 3'-CH), 4.65 (1H, dd, J = 11.8 Hz, 4.7 Hz), 5.04 (1H, br s, CHP), 5.17 (1H, tr, J = 2.0 Hz, CHP), 5.42 (1H, s, 4'-CH), 5.71 (1H, s, 1'-CH), 6.00 (1H, s, 1-CH), 6.48 (1H, d, J = 7.6 Hz, $NHCOCF_3$), 7.76 (2H, m, 7, 8-ArH), 8.10 (2H, m, 6, 9-ArH), 8.27 (2H, d, J = 8.0 Hz, PNB), 8.32 (2H, d, J = 8.0 Hz, PNB).

IR (Nicolet 205 FT, film on NaCl plate): cm^{-1}, 3323.0, 3242.5, 3077.6, 2965.0, 1730.3, 1661.9, 1593.5, 1529.2, 1271.8, 1193.2, 1050.8, 864.0, 835.7, 722.1.

The second compound, (1'S,1S,3R)-1-(2',3',6'-trideoxy-4'-p-niprobenzoyl-3'-trifluoroacetamido-L-lyxohexo pyranose)-3-dimethyl phosphonoacetyl-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho[2,3-c]-pyran had:

M.P. 135-137°C.

^1H NMR ($CDCl_3$, 250 MHz, Bruker): δ, 1.33 (3H, d, J = 6.4 Hz, 6'-CH_3), 2.01 (1H, br tr, J = 11.8 Hz, 3'-HCH_a), 2.15 (1H, br tr, J = 11.8 Hz, 3'-HCH_e), 2.62 (1H, dd, J = 18.8 Hz, 12.1 Hz, 4-HCH_a), 3.01 (1H, dd, J = 18.8 Hz, 4.4 Hz, 4-HCH_e), 3.81 (3H, s, $POCH_3$), 3.86 (3H, s, $POCH_3$), 4.58 (1H, m, 4'-CH), 4.60 (1H, dd, J = 12.1 Hz, 4.4 Hz, 3-CH), 4.79 (1H, qua, J = 6.4 Hz, 6-CH), 5.02 (1H, br s, PCH), 5.13 (1H, br s, PCH), 5.46 (1H, s, 5'-CH), 5.62 (1H, s, 1'-CH), 6.14 (1H, s, 1-CH), 6.63 (1H, d, J = 8.2 Hz, $NHCOCF_3$), 7.79 (2H, m, 7, 8-ArH), 8.16 (2H, m, 6, 9-ArH), 8.30 (4H, m, PNB).

IR (Nicolet 205 FT, film on NaCl plate): cm^{-1}, 3322.0, 3242.5, 3083.5, 2959.0, 2853.0, 1729.5, 1668.6, 1597.0, 1525.5, 1276.4, 1183.7, 1045.9, 853.9, 724.2.

Step 6: (1'S,1R,3S)-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3-dimethylphosphonoacetyl-5,10-dioxo-3,4,5-10-tetrahydro-1H-naphtho-[2,3-c]-pyran (BCH-1689)

The PNB-protected ketophosphonate from step 5 herein (21 mg, 0.028 mmol) was dissolved in THF-MeOH (3 ml of each) and cooled to 0°C. Sodium methoxide (4.3 m, 6.5 µl) was added. After stirred for 5 minutes at 0° C, the crude mixture (pink) was acidified with 0.1 N aqueous hydrogen chloride. It was extracted with methylene chloride, dried (over sodium sulfate) and evaporated to give a crude product which was recrystallized

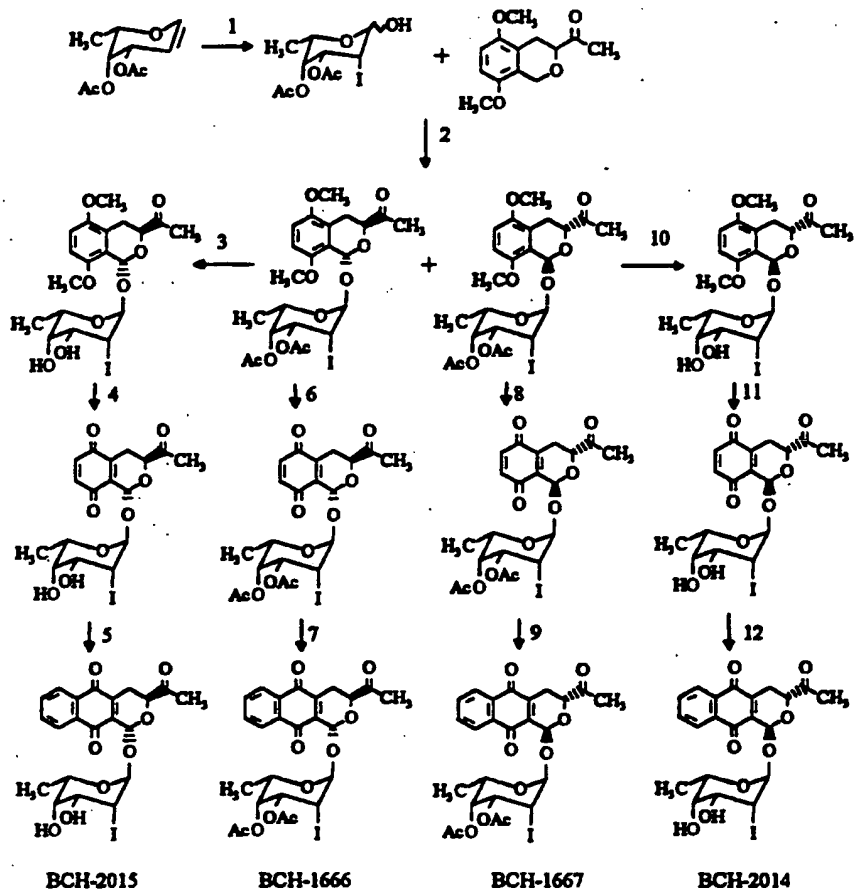
from methylene chloride and hexane to give the desired product (10 mg) as an off-white solid.

M.P. 95-97°C.

^{1}H NMR ($CDCl_3$, 250 MHz, Bruker): δ, 1.25 (3H, d, J = 8.2 Hz, 6'-CH_3), 1.83-1.98 (2H, m, 2'-CH_2), 2.53 (1H, dd, J = 17.6, 11.8 Hz, 4-HCH_a), 3.00 (1H, dd, J = 17.6 Hz, 3.5 Hz, 4-HCH_e), 3.62 (1H, br s, 4'-CH), 3.82 (3H, s, $POCH_3$), 3.86 (3H, s, $POCH_3$), 4.16 (1H, qua, J = 8.2 Hz, 5'-CH), 4.34 (1H, m, 3'-CH), 4.62 (1H, dd, J = 11.8 Hz, 3.5 Hz, 3-CH), 5.01 (1H, s, CHP), 5.12 (1H, s, CHP), 5.54 (1H, s, 1'-CH), 5.94 (1H, s, 1-CH), 6.82 (1H, d, J = 7.1 Hz, $NHCOCF_3$), 7.74 (2H, m, 7, 8-ArH), 8.06 (2H, m, 6, 9-ArH).

IR (Nicolet 205FT, film on NaCl plate): cm^{-1}, 3421.4 (br), 3080.8, 2960.1, 1718.4, 1664.5, 1556.7, 1457.6, 1283.0, 1188.1, 1043.7, 983.4, 858.9, 728.4.

Example 61: **Various C-2' axialy iodinated pyranylnaphthoquinone glycosides**



Step 1: **3,4-Di-O-acetyl-2-iodo-2,6-dideoxyfucose**

To a mixture of di-O-acetyl fucal (3.029 g, 14.140 mmol) in 180 ml of acetonitrile and 18 ml of water was added portionwise the NIS (3.590 g, 15.554 mmol). After stirring for 30 minutes the mixture was extracted with CH_2Cl_2 (2x) and the combined organic extracts were washed with 10% sodium thiosulfate solution, water and finally dried (Na_2SO_4) to give 4.403 g (87% yield) of the desired sugar.

PMR (acetone-d_6, 250 MHz) δ: 1.12 (d, 3H, J=6.4Hz, CH_3-6'), 1.99 and 2.11 (2s, 2X3H, 2XOAc), 4.36 (d, 1s, J=5.1Hz, H-2), 4.48 (q, 1H, J=6.6Hz, H-5), 4.98 (unresolved dd, 1H, H-3), 5.18 (broad s,1H, H-4), 5.59 (broad s, 1H, H-1), 5.94 (d, 1H, OH).

Step 2: **(1'S,1R,3S) and (1'S,1S,3R) - 2,5-Dimethoxy-1-(2',6'-dideoxy-3',4'-diacetoxy-2'-iodo-L-lyxohexopyranose)-3-acetoisochroman**

To a mixture of sugar from step 1 herein (910 mg, 2.539 mmol) and methyl ketone isochroman (500 mg, 2.116 mmol) in dry CH_2Cl_2 under argon atmosphere and room temperature was added some molecular sieve (4A). After stirring for 20 minutes DDQ (577 mg, 2.539 mmol) was added. After stirring for 72 hours, while additions of 0.5 equivalent of sugar and 0.5 equivalent of DDQ were done after 24 and 48 hours, the reaction was worked up by addition of 100 ml of $NaHCO_3$ 5% and water mixture (1:3). Extractions with CH_2Cl_2 (3x100 ml) following by washing with the same aqueous mixture and drying (Na_2SO_4). Flash chromatography of the crude (CH_2Cl_2:Hex:EtOAc; 9:4:1) gave 361 mg of the non-natural (1'S,1S,3R) glycoside and 435 mg of the natural (1'S,1R,3S) one. The arbitrarily assigned (1'S,1S,3R) titled compound had:
PMR (acetone-d_6, 250 MHz) δ: 1.27 (d,3H, J=6.5Hz, CH_3-6'), 1.94 and 2.16 (2s, 2X3H, 2XOAc), 2.30 (s,3H,$COCH_3$), 2.50 (dd, 1H, J=17.8Hz and 12.1Hz, CH_aCHO), 2.95 (dd, 1H, J=17.8 and 4.3Hz, CH_eCHO), 3.80 and 3.83 (2s, 2X3H, 2XOCH_3), 5.52 (d, 1H, J=5.0Hz, H-2'), 4.75 (m, 3H, H-3, H-3' and H-5'), 5.24 (broad s, 1H, H-4'), 5.89 (s, 1H, H-1'), 6.15 (s, 1H, H-1), 6.90 (2d, 2H, Ar-H).
The second (1'S,1S,3R) titled compound had:
PMR (acetone-d_6, 250 MHz) δ: 1.16 (d, 3H, J=6.6Hz, CH_3-6'), 1.97 and 2.15 (2s, 2X3H, 2XOAc), 2.30 (s, 3H, $COCH_3$), 2.45 (dd, 1H, J=17.6Hz and 12.2Hz, CH_aCHO), 2.96 (dd, 1H, J=17.6Hz and 4.1Hz, CH_eCHO), 3.80 and 3.82 (2s, 2X3H, 2XOCH_3), 4.48 (d, 1H, J=5.0Hz, H-2'), 4.54 (m, 2H, H-3, H-5'), 4.83 (unresolved dd, 1H, H-3'), 5.20 (broad s, 1H, H-4'), 5.86 (s, 1H, H-1'), 6.03 (s, 1H, H-1), 6.88 (2d, 2H, Ar-H).

Step 3: **(1'S,1R,3S)-5,8-Dimethoxy-3-aceto-1-(2',6'-dideoxy-2'-iodo-L-lyxohexopyranose)-isochroman**

To mixture of the compound from step 2 herein (500 mg, 0.844 mmol) in 90 ml of dry THF maintained at 0°C and under argon atmosphere were added 90 ml of NaOH 0.5N. After stirring for 1 hour the reaction mixture was neutralized with 160 ml of NH_4Cl sat.:$NaHCO_3$ sat. (4:1) and extracted with CH_2Cl_2 (3x200 ml). The combined organic layers were dried over

$MgSO_4$. Flash chromatography (toluene:ethyl acetate; 8:2) of the crude gave 248 mg (49% yield) of pure titled compound.
PMR (acetone-d_6, 250 MHz) δ: 1.26 (d, 3H, J=6.5Hz, CH_3-6'), 2.29 (s, 3H, $COCH_3$), 2.44 (dd, 1H, J=17.5Hz and 12.2Hz, CH_aCHO), 2.93 (dd, 1H, J=17.7Hz and 4.1Hz, CH_eCHO), 3.16 (d, 1H, J=6.0Hz, OH), 3.49 (m, 1H, H-3'), 3.77 (m, 1H, H-4'), 3.79 and 3.84 (2Xs, 2X3H, OCH_3), 4.09 (d, 1H, J=7.4Hz, OH), 4.25 (q, 1H, J=6.6Hz, H-5'), 4.37 (d, 1H, J=5.0Hz, H-2'), 4.54 (dd, 1H, J=12.2Hz, 4.1Hz, H-3), 5.84 (s, 1H, H-1'), 5.99 (s, 1H, H-1), 6.88 (2Xd, 2XH, ArH)

Step 4: (1'S,1R,3S)-3-aceto-1-(2',6'-dideoxy-2'-iodo-L-lyxohexopyranose)-5,8-dioxo-5,8-dihydroisochroman

The titled compound was obtained following CAN oxidation of the product from step 3 herein as per previous procedure.
PMR ($CDCl_3$, 250 MHz) δ: 1.32 (d, 3H, J=6.6Hz, CH_3-6'), 1.86 (large d, 1H, OH), 2.33 (s, 3H, $COCH_3$), 2.39 (dd, 1H, J=19.9 and 11.9Hz, CH_a-CHO), 2.81 (large s, 1H, OH), 2.90 (dd, 1H, J=19.7Hz and 3.9Hz, CH_e-CHO), 3.32 (large s, 1H, H-3'), 3.78 (large unresolved d, 1H, H-4'), 4.17 (broad q, 1H, J=5.0Hz, H-5'), 4.39 (m, 2H, H-3 and H-2'), 6.81 (s, 1H, H-1'), 6.89 (s, 1H, H-1), 6.81 (2Xd, 2H, quinone ring-H).
IR (film) ν_{max}: 3486, 3400, 2937, 1711, 1657, 1307, 968 cm^{-1}.

Step 5: (1'S,1R,3S)- methyl-(1-[2',6'-dideoxy-3',4'-dihydroxy-2'-iodo-L-lyxohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphtho [2,3-c]-pyran-3-yl) ketone (BCH-2015)

Starting from 50 mg (0.105 mmol) of the compound from step 4 herein and 1 ml of 1-acetoxybutadiene, the procedure described in step 2, example 5, has been followed. After purification, 15.8 mg (29% yield) of pure titled compound was isolated.
PMR ($CDCl_3$, 250 MHz) δ: 1.32 (d, 3H, J=6.7Hz, CH_3-6'), 1.91 (large d, 1H, J=11.0Hz, OH), 2.36 (s, 3H, $COCH_3$), 2.53 (dd, 1H, J=19.5Hz, 11.4Hz, CH_aCHO), 2.81 (large d, 1H, J=10.4Hz, OH), 3.08 (dd, 1H, J=19.9Hz and 4.1Hz, CH_eCHO), 3.34 (m, 1H, H-3'), 3.80 (m, 1H, H-4'), 4.17 (broad q, 1H, 6.9Hz, H-5'), 4.45 (m, 2H, H-3 and H-4'), 5.98 (2Xs, 2X1H, H-1 and H-1'), 7.78 and 8.11 (2Xm, 2X2H, ArH).
IR (film) ν_{max}: 3477 broad, 2928, 1722, 1670, 1298, 961, 732 cm^{-1}.

Step 6: (1'S,1R,3S)- 5,8-Dioxo-3-aceto-1-(2',6'-dideoxy-3',4'-diacetoxy-2'-iodo-L-lyxohexopyranose)-5,8-dihydroisochroman

CAN oxidation of the (1'S,1R,3S) diastereomeric product from step 2, example 61, yielded the titled compound.
PMR ($CDCl_3$, 250 MHz) δ: 1.21 (d, 3H, J=6.6Hz, CH_3-6'), 2.07 and 2.22 (2s, 2X3H, 2XOAc), 2.32 (s, 3H, $COCH_3$), 2.41 (dd, 1H, J=24.1Hz, 11.8Hz, CH_aCHO), 2.92 (dd, 1H, J=19.7Hz and 3.9Hz, CH_eCHO), 4.29 (q, 1H, J=6.5 Hz, H-5'), 4.36 (d, 1H, J=5.1Hz, H-2'), 4.41 (dd, 1H, J=11.2Hz and 4.0Hz, H-3), 4.78 (dd, 1H, J=4.0Hz, H-3'), 5.23 (broad s, 1H, H-4'), 5.82 (1s, 1H, H-1'), 5.87 (1s, 1H, H-1), 6.81 (2d, 2H, quinone ring-H).

Step 7: (1'S,1R,3S)-methyl-(1-[2',6'-dideoxy-3'-4'-diacetoxy-2'-iodo-L-lyxohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphtho [2,3-c]-pyran-3-yl) ketone (BCH-1666)

To a mixture of glycoside from step 6 herein (55 mg, 0.098 mmol) in 1.5 ml of dry toluene and under argon atmosphere, was added 1-acetoxybutadiene (66 mg, 0.587 mmol). After 18 hours of stirring the mixture was directly flash chromatographed (toluene:ethyl acetate; 9:1) to give 17 mg of pure titled compound (28% yield).
PMR (CD_2Cl_2, 250 MHz) δ: 1.20 (d, 3H, J=1.20Hz, CH_3-6'), 2.13 and 2.44 (2s, 2X3H, 2XOCH_3), 2.31 (s, 3H, $COCH_3$), 2.62 (dd, 1H, J=19.5Hz and 11.5Hz, HCH_aCHC=O), 3.16 (dd, 1H, J=19.5Hz, 4.0Hz, HCH_eCHC=O), 4.45 (broad q, 1H, J=6.6Hz, H-5'), 4.51 (d, 1H, J=5.0Hz, H-2'), 4.62 (unresolved dd, 1H, J=11.7Hz and 4.0Hz, H-3), 4.88 (dd, 1H, J=4.0Hz, H-3'), 5.32 (broad s, 1H, H-4'), 6.06 (s, 1H, H-1'), 6.16 (s, 1H, H-1), 7.71 and 8.22 (2m, 2X2H, ArH).
IR (film) ν_{max}: 2991, 2935, 1746, 1668, 1238, 970, 730 cm^{-1}.

Step 8: (1'S,1S,3R)-5,8-Dioxo-3-aceto-1-(2',6'-dideoxy-3',4'-diacetoxy-2'-iodo-L-lyxohexopyranose)-5,8-dihydroisochroman

CAN oxidation of the (1'S,1S,3R) glycoside from step 2, example 61, gave the titled compound.
PMR ($CDCl_3$, 250 MHz) δ: 1.35 (d, 3H, J=6.6Hz, CH_3-6'), 2.07 and 2.23 (2s, 2X3H, 2XOAc), 2.32 (s, 3H, $COCH_3$), 2.46 (dd, 1H, J=20.3 Hz and 11.7 Hz, CH_aCHO), 2.90 (dd, 1H, J=19.7Hz and 4.1Hz, CH_eCHO), 4.25 (d, 1H, J=5.2Hz, H-2'), 4.43 (dd, 1H, J=11.6Hz and 4.1Hz, H-3), 4.61 (q, 1H,

J=6.2Hz, H-5'), 4.75 (dd, 1H, J=3.6 Hz, H-3'), 5.26 (broad s, 1H, H-4'), 5.82 (s, 1H, H-1'), 5.97 (s, 1H, H-1), 6.81 (2d, 2H, quinone ring-H).

IR (film) ν_{max}: 2945, 1747 broad, 1663, 1237, 969 cm^{-1}.

Step 9: (1'S,1S,3R)-methyl-(1-[2',6'-dideoxy-3',4'-diacetoxy-2'-iodo-L-lyxohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphtho [2,3-c]-pyran-3-yl) ketone (BCH-1667)

Starting from 70 mg (0.118 mmol) of compound from step 8 herein and 79.6 mg of 1-acetoxybutadiene and following the procedure described in step 2, example 5, we obtained after purification 25 mg (35% yield) of titled compound.

PMR ($CDCl_3$, 250 MHz) δ: 1.40 (d, 3H, J=6.4 Hz, CH_3-6'), 2.05 and 2.24 (2s, 2x3H, 2xOCH_3), 2.35 (s, 3H, $COCH_3$), 2.57 (dd, 1H, J=20.0 and 12.4Hz, HCH_aCHCO), 3.07 (dd, 1H, J=20.0Hz and 4.2Hz, $HCH_eCHC=O$), 4.27 (d, 1H, J=5.0Hz, H-2'), 4.49 (dd, 1H, J=11.6, 4.2 Hz, H-3), 4.75 (m, 2H, H-3' and H-5'), 5.28 (large s, 1H, H-4'), 5.86 (s, 1H, H-1'), 6.14 (s, 1H, H-1), 7.77 and 8.11 (2m, 2X2H, ArH).

IR (film) ν_{max}: 2945, 1743 broad, 1668, 1236 broad, 958, 734 cm^{-1}.

Step 10: (1'S,1S,3R)-5,8-Dimethoxy-3-aceto-1-(2',6'-dideoxy-2'-iodo-L-lyxohexopyranose)-isochroman

The titled compound was obtained via base hydrolysis of the (1'S,1S,1R) precursor from step 2 herein as per procedure from step 3 herein.

PMR (acetone-d_6, 250 MHz) δ: 1.35 (d, 3H, J=6.6Hz, CH_3-6'), 2.30 (s, 3H, $COCH_3$), 2.50 (dd, 1H, J=17.6 and 11.5 Hz, CH_aCHO), 2.94 (dd, 1H, J=17.9 and 4.3Hz, CH_eCHO), 3.20 (d, 1H, OH), 4.44 (m, 1H, H-3'), 3.80 (large s, 7H, 2XOCH_3 and H-4'), 4.12 (d, 1H, OH), 4.41 (d, 1H, J=5.0Hz, H-2'), 4.55 (q, 1H, J=6.4Hz, H-5'), 4.70 (dd, 1H, J=12.1 Hz and 4.5 Hz, H-3), 5.87 (1S, 1H, H-1'), 6.14 (1s, 1H, H-1), 6.88 (2d, 2H, ArH).

Step 11: (1'S,1S,3R)-3-aceto-1-(2',6'-dideoxy-2'-iodo-L-lyxohexopyranose)-5,8-dioxo-5,8-dihydroisochroman

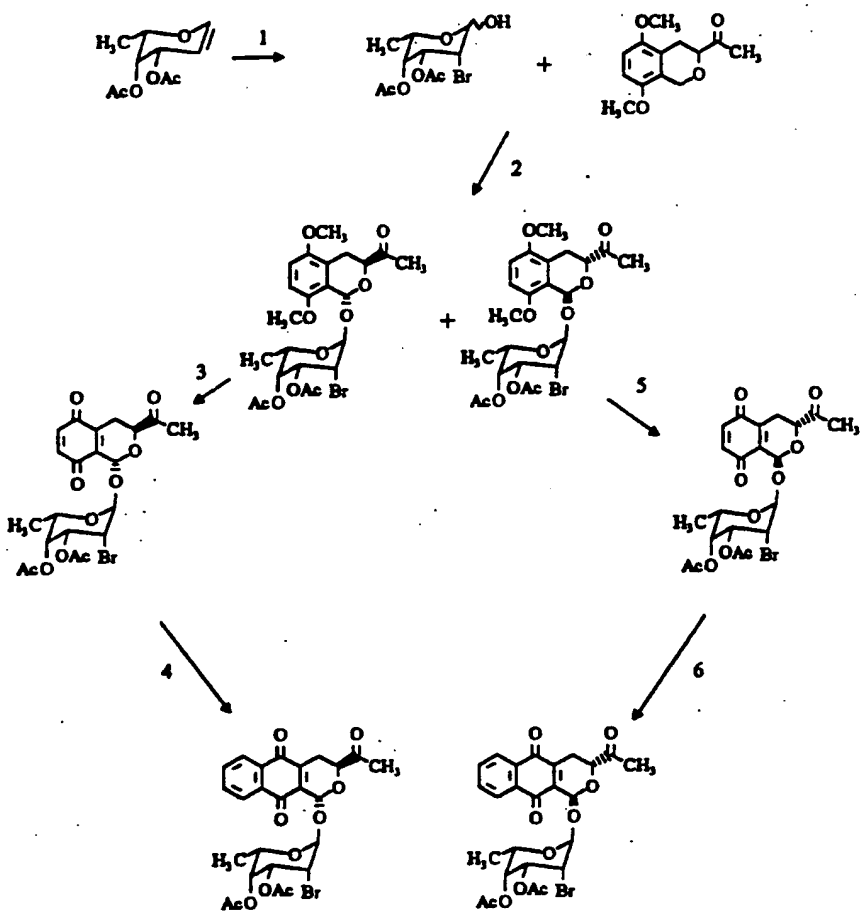
The titled compound was obtained following CAN oxidation of the product from step 10 herein as per previous procedure.

PMR ($CDCl_3$, 250 MHz) δ: 1.45 (d, 3H, J=6.6Hz, CH_3-6'), 1.90 (broad s, 1H, OH), 2.31 (s, 3H, $COCH_3$), 2.43 (dd, 1H, J=20.1Hz and 11.8 Hz, CH_aCHO), 2.80 (m, 1s, OH), 2.88 (dd, 1H, J=19.8Hz and 4.1Hz, CH_eCHO), 3.32 (m, 1H, H-3'), 3.84 (m, 1H, H-4'), 4.24 (d, 1H, J=4.4Hz, H-2'), 4.42 (dd, 1H, J=11.8Hz and 4.2Hz, H-3), 5.82 (s, 1H, H-1'), 5.95 (s, 1H, H-1), 6.79 (2Xd, 2H, quinone ring-H).

Step 12: (1'S,1S,3R)-methyl-(1-[2',6'-dideoxy-3',4'-dihydroxy-2'-iodo-L-lyxohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphtho [2,3-c]-pyran-3-yl)-ketone (BCH-2014)

A mixture of compound from step 11 herein (1 ml) and 1-acetoxy-butadiene (96 mg, 0.201 mmol) in 2 ml of dry toluene was stirred for 18 hours under argon atmosphere and then flash chromatographed (Toluene:Ethyl acetate; 8:2) to give 42 mg (40% yield) of pure titled compound.
PMR ($CDCl_3$, 250 MHz) δ: 1.52 (d, 3H, CH_3-6'), 2.36 (s, 3H, $COCH_3$), 2.58 (dd, 1H, J=19.7Hz and 11.4Hz, HCH_aCHCO), 2.78 (broad m, 1H, OH), 3.09 (dd, 1H, J=20.0Hz and 4.2Hz, HCH_eCHCO), 3.34 (m, 1H, H-3'), 3.89 (m, 1H, H-4'), 4.27 (d, 1H, J=4.5Hz, H-2'), 4.49 (dd, 1H, J=11.7Hz and 4.2Hz, H-3), 4.66 (broad q, 1H, J=6.4Hz, H-5'), 5.30 (s, 1H, H-1'), 5.89 (s, 1H, H-1), 7.53 and 8.13 (2m, 2X2H, Ar-H).
IR (film) ν_{max}: 3434 broad, 2934 broad, 1720, 1669, 1292, 995, 955 cm^{-1}.

Example 62: **Various C-2' axialy brominated pyranylnaphthoquinone glycosides**



Step 1: **3,4-Di-O-acetyl-2-bromo-2,6-dideoxyfucose**

Following the procedure described in step 1, example 61, we obtained after work-up 89% yield of a mixture of four compounds. Probably axial and equatorial bromo sugars and α and β isomers of each.

Step 2: **(1'S,1R,3S) and (1'S,1S,3R)-2,5-Dimethoxy-1-(2',6'-dideoxy-3',4'-diacetoxy-2'-bromo-L-lyxohexopyranose)-3-acetoisochroman**

Following the procedure described in step 2, example 61, we obtained after purification (Dichloromethane:Hexane:Ethyl acetate; 12:7:1) 35% yield of a separable (1'S,1R,3S and 1'S,1S,3R) 1:1 mixture of titled diastereoisomers.

(1'S,1S,3R): PMR (acetone-d_6, 250 MHz) δ: 1.27 (d, 3H, J=6.5Hz, CH_3-6'), 1.94 and 2.11 (2Xs, 2X3H, 2XOAc), 2.29 (s, 3H, $COCH_3$), 2.50 (dd, 1H, J=17.7Hz and 12.1Hz, CH_aCHO), 2.96 (dd, 1H, J=17.8 and 4.2Hz, CH_eCHO), 3.80 and 3.84 (2Xs, 2X3H, $2XOCH_3$), 4.42 (d, 1H, J=4.2Hz, H-2'), 4.71 (dd, 1H, J=12.2Hz and 4.2 Hz,H-3), 4.81 (q, 1H, J=6.4Hz, H-5'), 5.22 (m, 2H, H-3' and H-4'), 5.74 (s,1H, H-1'), 6.17 (s, 1H, H-1), 6.90 (2Xd, 2H, Ar-H).

IR (film) ν_{max}: 2937, 1748, 1486, 1260 and 1237, 970 cm^{-1}.

(1'S,1R,3S): PMR (acetone, 250 MHz) δ: 1.16 (d, 3H, J=6.6Hz, CH_3-6'), 1.97 and 2.10 (2Xs, 2X3H, 2XOAc), 2.30 (s, 3H, $COCH_3$), 2.45 (dd, 1H, J=17.6Hz and 12.2Hz, CH_aCHO), 2.97 (dd, 1H, J=17.6Hz and 4.0Hz, CH_eCHO), 3.80 and 3.82 (2Xs, 2X3H, $2XOCH_3$), 4.38 (d, 1H, J=4.6Hz, H-2'), 4.53 (q, 1H, J=6.4Hz, H-5'), 5.16 (broad s, 1H, H-4'), 5.27 (dd, 1H, J=4.2Hz, H-3'), 5.71 (s, 1H, H-1'), 6.05 (s, 1H, H-1), 6.89 (2Xd, 2H, Ar-H).

Step 3: (1'S,1R,3S)-5,8-dioxo-1-(2',6'-dideoxy-3',4'-diacetoxy-2'-bromo-L-lyxohexopyranose)-5,8-dihydroisochroman

CAN oxidation of the compound from step 2 herein yielded the titled compound.

PMR ($CDCl_3$, 250 MHz) δ: 1.19 (d, 3H, J=6.6Hz, CH_3-6'), 2.04 and 2.16 (2Xs, 2X3H, 2XOAc), 2.29 (s, 3H, $COCH_3$), 2.38 (dd, 1H, J=19.9Hz and 11.6Hz, CH_aCHO), 2.88 (dd, 1H, J=19.8Hz and 3.9Hz, CH_eCHO), 4.25 (m, 2H, H-2' and H-5'), 4.39 (dd, 1H, J=11.6Hz and 3.8Hz, H-3), 5.16 (broad s, 1H, H-4'), 5.19 (dd, 1H, J=4.0Hz, H-3'), 5.71 (s, 1H, H-1'), 5.81 (s, 1H,H-1), 6.79 (2Xd, 2H, Ar-H).

Step 4: (1'S,1R,3S)-methyl-(1-[2',6'-dideoxy-3',4'-diacetoxy-2'-bromo-L-lyxohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-c]-pyran-3-yl) ketone (BCH-2100)

The titled compound was obtained following the procedure described in step 2, example 5, from the compound from step 3 herein. HPLC purification gave 9% of desired (1'S,1R,3S) natural titled glycoside.

PMR ($CDCl_3$, 250 MHz) δ: 1.23 (d, 3H, J=6.4Hz, CH_3-6'), 2.06 and 2.19 (2s,2X3H, 2XOAc), 2.35 (s, 3H, $COCH_3$), 2.54 (dd, 1H, J=19.7Hz and 11.7Hz, CH_aCHO), 3.09 (dd, 1H, J=19.8Hz and 4.0Hz, CH_eCHO), 4.29 (m, 2H, H-2' and H-5'), 4.47 (dd, 1H, J=11.7Hz and 4.0Hz, H-3), 5.18 (broad s,

1H, H-4'), 5.23 (unresolved dd, 1H, H-3'), 5.83 (s, 1H, H-1'), 6.01 (s, 1H, H-1), 7.77 and 8.11 (2m, 2X2H, Ar-H).
IR (film) ν_{max}: 2991 and 2943, 1748,1665, 1241, 975 cm^{-1}.

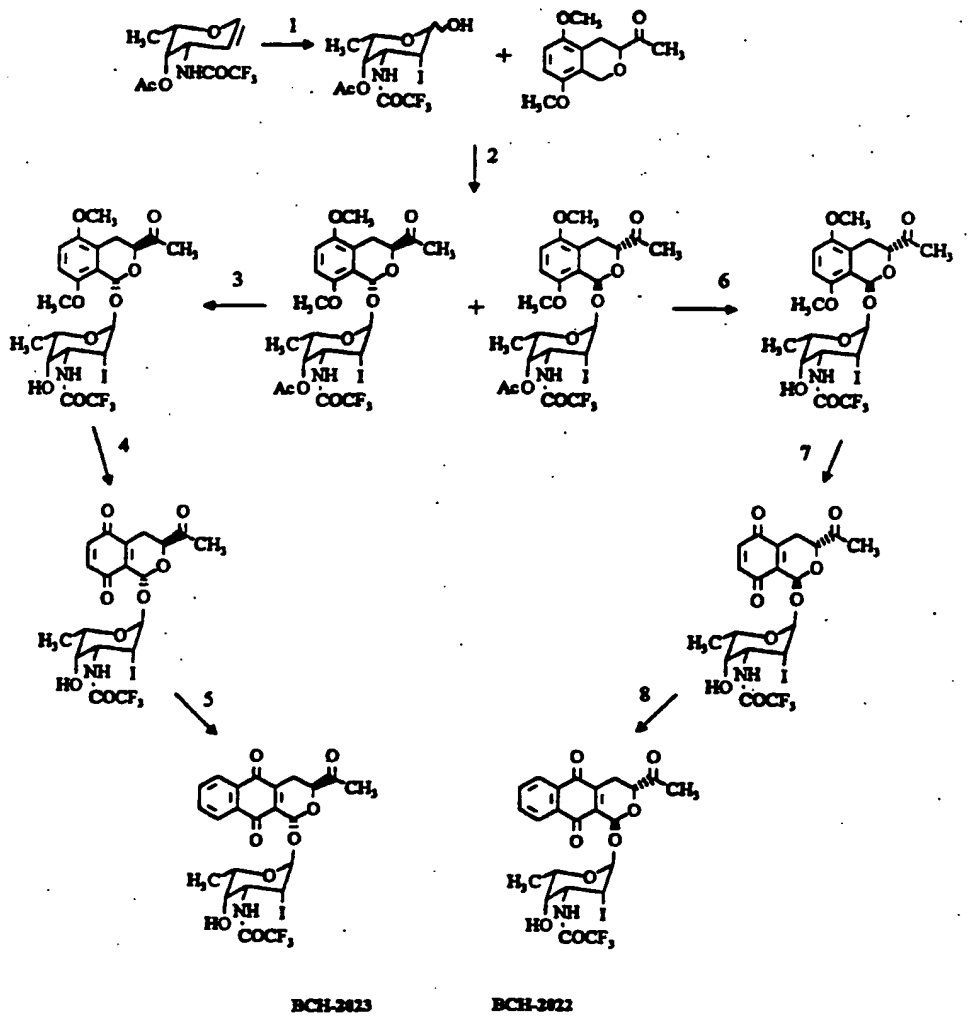
Step 5: (1'S,1R,3S)-5,8-dioxo-3-aceto-1-(2',6'-dideoxy-3',4'-diacetoxy-2'-bromo-L-lyxohexopyranose)-5,8-dihydroisochroman

CAN oxidation of the (1'S,1R,3S) diasterecmer from step 2 herein yielded the titled product.
IR (film) ν_{max}: 2939, 1743, 1674, 1241, 968 cm^{-1}.

Step 6: (1'S,1S,3R)-methyl-(1-[2',6'-dideoxy-3',4'-diacetoxy-2'-bromo-L-lyxohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-c]-pyran-3-yl) ketone (BCH-2099)

The titled compound was obtained following the procedure described in step 2, example 5, from the quinone from step 5 herein. Flash chromatography (Toluene:Ethyl acetate; 9:1) gave 30% of desired titled compound.
PMR ($CDCl_3$, 250 MHz) δ: 1.41 (d, 3H, J=6.4Hz, CH_3-6'), 2.05 and 2.21 (2s, 2X3H, 2XOAc), 2.34 (s, 3H, $COCH_3$), 2.58 (dd, 1H, J=20.1Hz and 11.6Hz, CH_aCHO), 3.08 (dd, 1H, J=20.0Hz and 4.2Hz, CH_eCHO), 4.16 (d, 1H, J=4.5Hz, H-2'), 4.48 (dd, 1H, J=11.6Hz and 4.1Hz, H-3), 4.76 (q, 1H, J=5.9Hz, H-5'), 5.20 (unresolved dd, 1H, H-3'), 5.25 (broad s, 1H, H-4'), 5.72 (1s, 1H, H-1'), 6.17 (1s, 1H, H-1), 7.78 and 8.12 (2m, 2X2H, Ar-H).
IR (film) ν_{max}: 2937, 1750, 1672, 1243, 964 cm^{-1}.

Example 63: C-2'-axialy iodinated daunosaminyl pyranylnaphthoquinone glycosides



Step 1: 2',3',6'-trideoxy-2'-iodo-3'-trifluoroacetamido-4'-O-acetyl-L-lyxohexopyranose

Following the procedure described in step 1, example 61, we obtained after work-up 94% yield of a non-separable α-β mixture (2:1) of titled halogenated sugar.

PMR (acetone-d_6, 250 MHz) δ: 1.08 (d, 3H, J=6.6Hz, CH_3-6), 2.13 (s, 3H, OAc-4), 4.47 (m, 1H, H-3), 4.53 (d, 1H, J=4.3Hz, H-2), 4.56 (broad q, 1H, J=5.2Hz, H-5), 5.17 (broad s, 1H, H-4), 5.65 (d, 1H, J=3.8Hz, H-1), 6.04 (d, 1H, J=3.8Hz, OH).

Step 2: (1'S,1R,3S) and (1'S,1S,3R)-2,5-Dimethoxy-3-aceto-1-(2',3',6'-trideoxy-2'-iodo-3'-trifluoroacetamido-4'-O-acetyl-L-lyxohexopyranose)-isochroman

Following the same procedure as described in step 2, example 61, we obtained after purification (Toluene:Ethyl acetate; 9:1) 38% yield of a separable (1'S,1R,3S and 1'S,1S,3R) mixture of titled diastereoisomers (1:1).

The natural (1'S,1R,3S) glycoside: PMR (acetone-d_6, 250 MHz) δ: 1.16 (d, 3H, J=6.6Hz, CH_3-6'), 2.15 (s, 3H, AcO-4'), 2.30 (s, 3H, $COCH_3$), 2.41 (unresolved dd, 1H, CH_aCHCO), 2.97 (dd, 1H, J=17.7Hz and 3.89Hz, CH_eCHO), 3.80 and 3.84 (2xs, 2x3H, 2xOCH_3), 4.36 (m, 1H, H-3'), 4.63 (m, 3H, H-3, H-2' and H-5'), 5.19 (broad s, 1H, H-4'), 5.90 (s, 1H, H-1'), 6.06 (s, 1H, H-1), 6.87 (2xd, 2H, Ar-H), 7.95 (broad s, 1H, $NHCOCF_3$).

The non-natural glycoside (1'S,1S,3R): PMR (acetone-d_6, 250 MHz) δ: 1.23 (s, 3H, J=6.5Hz, CH_3-6'), 2.16 (s, 3H, AcO-4'), 2.30 (s, 3H, $COCH_3$), 2.51 (dd, 1H, J=18.2Hz and 12.0Hz, CH_aCHO), 2.97 (dd, 1H, J=17.8Hz and 4.3Hz, CH_eCHO), 3.80 and 3.83 (2Xs, 2X3H, 2XOCH_3), 4.30 (m, 1H, H-3'), 4.69 (d, 1H, J=4.72Hz, H-2'), 4.74 (dd, 1H, J=12.1Hz and 4.3Hz, H-3), 4.88 (q, 1H, J=5.0Hz, H-5'), 5.24 (broad s, 1H, H-4'), 5.92 (s, 1H, H-1'), 6.18 (s, 1H, H-1), 6.90 (2Xd, 2X1H, Ar-H), 7.95 (broad s, 1H, $NHCOCF_3$).

Step 3: (1'S,1R,3S)-5,8-Dimethoxy-3-aceto-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-2'-iodo-L-lyxohexopyranose)-isochroman

Base hydrolysis of the compound from step 2 herein as per procedure from step 3, example 61, yielded the titled compound. PMR (acetone-d_6, 250 MHz) δ: 1.28 (d, 3H, J=6.6Hz, CH_3-6'), 2.30 (s, 3H, $COCH_3$), 2.45 (dd, 1H, J=17.6Hz and 12.2Hz, CH_aCHO), 2.95 (dd, 1H, J=17.6Hz and 4.0Hz, CH_eCHO), 3.79 and 3.84 (2s, 2X3H, 2XOCH_3), 4.03 (m, 2H, H-4' and OH-4'), 4.44 (broad q, 1H, J=6.4Hz, H-5'), 4.58 (m, 2H, H-3 and H-2'), 5.89 (s, 1H, H-1'), 6.04 (s, 1H, H-1), 6.89 (2d, 2XH, Ar-H), 7.65 (broad s, 1H, $NHCOCF_3$).

IR (film) ν_{max}: 3539 and 3414, 2941 and 2844, 1728, 1488, 1260, 1175, 970 cm^{-1}.

Step 4: (1'S,1R,3S)-3-aceto-1-(2',3',6'-trideoxy -2'-iodo-3'-trifluoroacetamido-L-lyxohexopyranose)-5,8-dioxo-5,8-dihydroisochroman

CAN oxidation of the product from step 3 herein yielded the titled product.

PMR ($CDCl_3$, 250 MHz) δ: 1.32 (d, 3H, J=6.6Hz, CH_3-6'), 2.06 (broad d, 1H, OH-4'), 2.32 (s, 3H, $COCH_3$), 2.41 (dd, 1H, J=20.4Hz and 11.7Hz, CH_aCHO), 2.93 (dd, 1H, J=19.6 and 3.9Hz, CH_eCHO), 3.75 (broad d, 1H, H-4'), 3.96 (m, 1H, H-3'), 4.28 (q, 1H, J=6.7Hz, H-5'), 4.42 (m, 2H, H-3 and H-2'), 5.82 (s, 1H, H-1'), 5.90 (s, 1H, H-1), 6.82 (2xd, 2H, Ar-H), 7.06 (broad d, 1H, $NHCOCF_3$).

IR (film) ν_{max}: 3541 and 3417, 2992 and 2944, 1729, 1664, 1174, 967 cm^{-1}.

Step 5: (1'S,1R,3S)-methyl-(1-[2',3',6'-trideoxy-2'-iodo-3'-trifluoroacetamido-4'-hydroxy-L-lyxohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-c]-pyran-3-yl) ketone (BCH-2023)

The titled compound was obtained as per procedure described in step 2, example 5, but using the product from step 4 herein. Purification was effected by flash chromatography (Toluene:Ethyl acetate; 8:2).

PMR ($CDCl_3$, 250 MHz) δ: 1.34 (d, 3H, J=6.6Hz, CH_3-6'), 2.35 (s, 3H, $COCH_3$), 2.53 (dd, 1H, J=19.6Hz and 11.5Hz, CH_aCHO), 3.11 (dd, 1H, J=19.6Hz and 4.1Hz, CH_eCHO), 3.76 (broad s, 1H, H-4'), 3.97 (m, 1H, H-3'), 4.30 (q, 1H, J=6.6Hz, H-5'), 4.49 (dd+d, 2H, H-3 and H-2'), 6.00 (1s, 2H, H-1 and H-1'), 7.01 (broad d, 1H, $NHCOCF_3$), 7.78 and 8.13 (2Xm, 2X2H, Ar-H).

IR (film) ν_{max}: 3529 and 3414, 2991 and 2930, 1727, 1666, 1298, 1177, 963 cm^{-1}.

Step 6: (1'S,1S,3R)-5,8-dimethoxy-3-aceto-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-2'-iodo-L-lyxohexopyranose) isochroman

To a mixture of (1'S,1S,3R) glycoside from step 2 herein (103 mg, 0.16 mmol) in 15 ml of anhydrous methanol was added, at 0°C and under argon atmosphere, 2 drops of $NaOCH_3$, 4.37M (cat.). After stirring for 45 minutes, the reaction was worked up by adding 10 ml of a mixture NH_4Cl sat.:$NaHCO_3$ sat. (8:3) and extracted with CH_2Cl_2 (2x30 ml). The combined organic layers were washed with the same aqueous mixture (30 ml) and dried ($MgSO_4$). Flash chromatography (Toluene:Ethyl acetate; 9:1) gave 70 mg of pure titled glycoside (73% yield).

PMR (acetone-d_6, 250 MHz) δ: 1.38 (d, 3H, J=6.5Hz, CH_3-6'), 2.30 (s, 3H, $COCH_3$), 2.50 (dd, 1H, J=17.7Hz and 12.0Hz, CH_aCHO), 2.97 (dd, J=17.8Hz and 4.3Hz, CH_eCHO), 3.80 and 3.81 (2Xs, 2X3H, $2XOCH_3$), 4.00 (m, 3H, H-3', H-4' and OH-4'), 4.62 (d, 1H, J=4.8Hz, H-2'), 4.74 (m, 2H, H-3 and H-5'), 5.92 (1s, 1H, H-1'), 6.18 (1s, 1H, H-1), 6.88 (2Xd, 2H, Ar-H), 7.65 (broad s, 1H, $NHCOCF_3$).
IR (film) ν_{max}: 3530, 3410, 2942 and 2837, 1723 broad, 1491, 1263, 1175, 958 cm^{-1}.

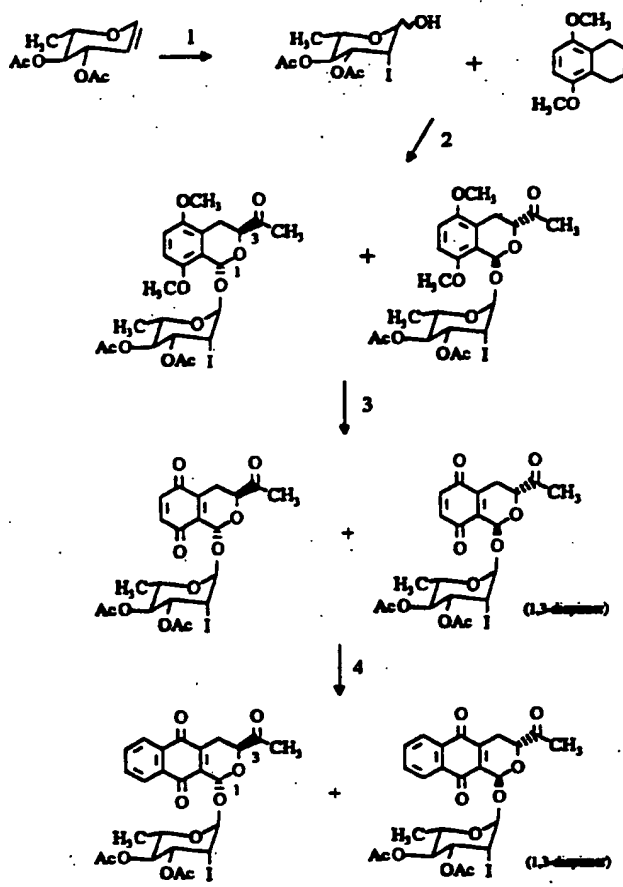
Step 7: (1'S,1S,3R)-3-aceto-1-(2',3',6'-trideoxy-2'-iodo-3'-trifluoroacetamido-L-lyxohexopyranose)-5,8-dioxo-5,8-dihydroisochroman

CAN oxidation of the product from step 6 herein yielded the titled product.
PMR ($CDCl_3$, 250 MHz) δ: 1.47 (d, 3H, J=6.61Hz, CH_3-6'), 2.22 (broad d, 1H, OH-4'), 2.32 (1s, 3H, $COCH_3$), 2.46 (dd, 1H, J=19.6Hz and 11.7Hz, CH_aCHO), 2.92 (dd, 1H, J=19.9Hz and 4.2Hz), 3.78 (broad d, 1H, H-4'), 3.91 (m, 1H, H-3'), 4.37 (d, 1H, J=4.8Hz, H-2'), 4.43 (dd, 1H, J=11.7Hz and 4.1Hz, H-3), 4.64 (q, 1H, J=6.3Hz, H-5'), 5.84 (s, 1H, H-1'), 5.97 (s, 1H, H-1), 6.82 (2xd, 2H, Ar-H), 7.06 (broad d, 1H, $NHCOCF_3$).
IR (film) ν_{max}: 3531 and 3406, 2929, 1726, 1663, 1181 broad, 960 cm^{-1}.

Step 8: (1'S,1S,3R)-methyl-(1-[2',3',6'-trideoxy-2'-iodo-3'-trifluoroacetamido-4'-hydroxy-L-lyxohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-c]-pyran-3-yl) ketone (BCH-2022)

The titled compound was obtained as per procedure described in step 2, example 5, but using the product from step 7 herein. Purification by flash chromatography (Toluene:Ethyl acetate; 9:1).
PMR ($CDCl_3$, 250 MHz) δ: 1.51 (d, 3H, J=6.5Hz, CH_3-6'), 2.11 (broad d, 1H, OH-4'), 2.34 (s, 3H, $COCH_3$), 2.58 (dd, 1H, J=19.4Hz and 11.6Hz, CH_aCHO), 3.10 (dd, 1H, J=19.8Hz and 4.1Hz, CH_eCHO), 3.82 (broad d, 1H, H-4'), 3.92 (dd, 1H, J=11.6Hz and 4.1Hz, H-3), 4.79 (q, 1H, J=6.5Hz, H-5'), 5.88 (s, 1H, H-1'), 6.14 (s, 1H, H-1), 7.07 (broad d, 1H, $NHCOCF_3$), 7.78 and 8.11 (2Xm, 2X2H, Ar-H).
IR (film) ν_{max}: 3539 and 3414, 2946, 1731, 1666, 1293, 1174, 961 cm^{-1}.

Example 64:



BCH-2065

Step 1: 2',6'-dideoxy-3',4'-diacetoxy-2'-iodo-L-arabinohexopyranose

Following the procedure described in step 1, example 61, we obtained after work-up a quantitative yield of the desired compound which was used in the next step without purification:

PMR (Benzene-d_6, 250 MHz) δ: 1.17 (d, 3H, J=6.2Hz, CH_3-6), 4.04 (m, 1H, H-5), 4.48 (d, 1H, J=4.2Hz, H-2), 4.84 (dd, 1H, J=9.5Hz and 4.2Hz, H-3), 5.01 (large s, 1H, H-1), 5.51 (dd, 1H, J=9.7Hz, H-4).

Step 2: (1'S,1S,3R) and (1'S,1R,3S)-5,8-Dimethoxy-3-aceto-1-(2',6'-dideoxy-3',4'-diacetoxy-2'-iodo-L-arabinohexopyranose) isochroman

Following the same procedure as described in step 2, example 61, we obtained after flash chromatography (Toluene:Ethyl acetate; 9:1) a mixture of the titled stereoisomers (non-separable).
PMR (Benzene-d_6, 250 MHz) δ: 1.20 and 1.38 (2d, 2X3H, $2XCH_3$-6'), 1.61, 1.66, 1.67 and 1.69 (4s, 4X3H, 4XOAc), 1.95 and 2.12 (2s, 2X3H, $2XOCH_3$), 2.76 (m, 2XH, $2XCH_aCHO$), 3.20 (m, 2H, $2XCH_eCHO$), 2.30, 2.31 and 2.32 (3s, 4X3H, $4XOCH_3$), 4.18 (m, 1H, H-5'), 4.35 and 4.47 (2Xdd, 2H, J=12.0Hz and 4.2Hz, 2XH-3), 4.82 (m, 5H, 2XH-3', 2XH-2'; and H-5'), 5.62 and 5.70 (2Xdd, 2H, J=9.5Hz, 2XH-4'), 5.84 and 5.93 (2 large s, 2H, 2XH-1'), 5.95 (s, 1H, H-1), 6.33 (m, 5H, 2X2 Ar-H and H-1).

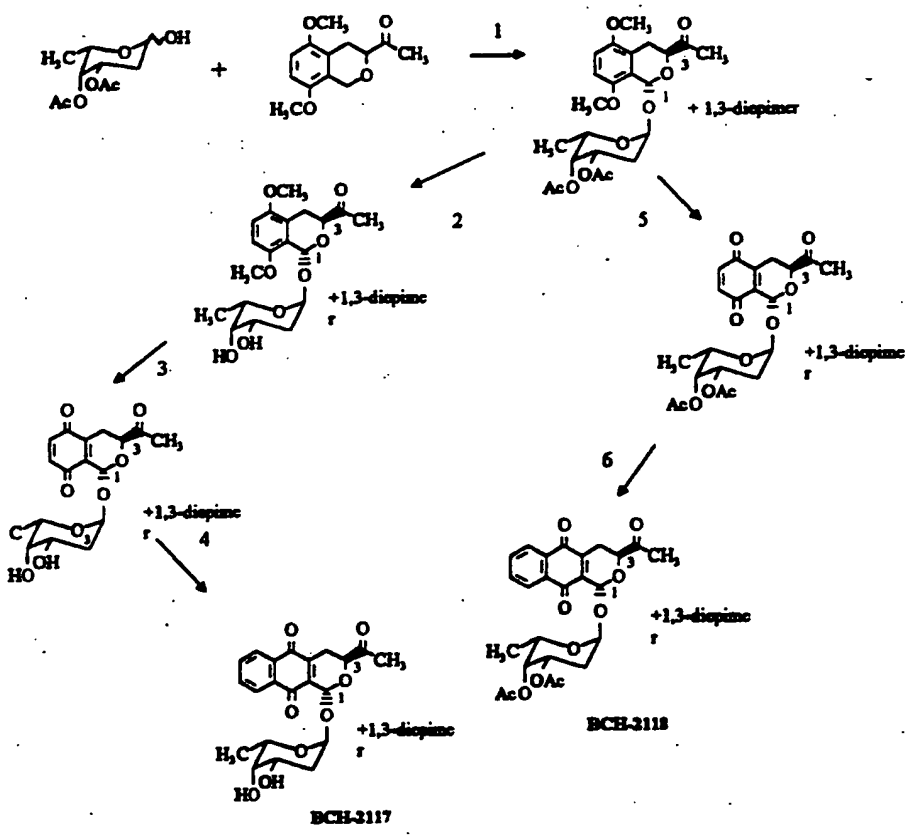
Step 3: (1'S,1R,3S) and (1'S,1S,3R)-3-aceto-1-(2',6'-dideoxy-2'-iodo-L-arabinohexopyranose)-5,8-dioxo-5,8-dihydroisochroman

The titled compounds were obtained following CAN oxidation of the products from step 2 herein as per previous procedures.
PMR ($CDCl_3$, 250 MHz) δ: 1.23 and 1.36 (2d, 2X3H, J=6.2Hz, $2XCH_3$-6'), 2.03, 2.04, 2.06 and 2.07 (4s, 4X3H, 4XOAc), 2.29 and 2.30 (2S, 2X3H, $2XCOCH_3$), 2.46 (m, 2H, $2XCH_aCHO$), 2.90 (dd, 2H, J=19.7Hz and 3.8Hz, $2XCH_eCHO$), 4.02 (m, 1H, H-5'), 4.49 (m, 7H, 2XH-2', 2XH-3', 2XH-3 and H-5'), 5.15 (m, 2H, 2XH-4'), 5.62 and 5.68 (2S, 2H, 2XH-1'), 5.79 and 5.95 (2s, 2H, 2XH-1), 6.75 (2X2d, 4H, 4XAr-H).

Step 4: (1'S,1R,1S) and (1'S,1S,3R)-methyl-(1-[2',6'-dideoxy-3',4'-diacetoxy-2'-iodo-L-arabino-hexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-c]-pyran-3-yl) ketone (BCH-2065)

Following the reported procedure in step 2, example 5, and starting from the two stereoisomers from step 3 herein, titled compounds (9%) were isolated after flash chromatography (Toluene:Ethyl acetate; 19:1).
PMR ($CDCl_3$, 250 MHz) δ: 1.41 (d, 3H, J=6.2Hz, CH_3-6'), 2.06 and 2.08 (2s, 2X3H, 2XOAc), 2.33 (s, 3H, $COCH_3$), 2.57 (dd, 1H, J=19.5Hz and 11.7Hz, CH_aCHO), 3.09 (dd, 1H, J=19.8Hz and 4.2Hz, CH_eCHO), 4.46 (m, 4H, H-3, H-2', H-3' and H-5'), 5.21 (dd, 1H, J=9.5Hz, H-4'), 5.67 (s, 1H, H-1'), 6.14 (s, 1H, H-1), 7.78 and 8.13 (2m, 2X2H, Ar-H).
IR (film) ν_{max}: 2941, 1750 and 1739, 1665, 1298, 1236 large, 971 cm^{-1}.

Example 65: C-2' deoxyfucose pyranylnaphthoquinone glycosides



Step 1: (1'S,1S,3R) and (1'S,1R,3S)-5,8-dimethoxy-3-aceto-1-(2',6'-dideoxy-3',4'-diacetoxy-L-lyxohexopyranose) isochroman

The procedure described in step 2, example 61, was applied to 5,8-dimethoxy-3-acetoisochroman and 3,4-diacetoxy-2,6-dideoxy fucose. Flash chromatography (dichloromethane:Hexane:Ethyl acetate; 6:3:1) gave a 50% yield of the two non-separable titled stereoisomers mixture (1:1). PMR (acetone-d_6, 250 MHz) δ: 1.11 and 1.20 (2d, 2X3H, J=6.6Hz, CH_3-6'), 1.87, 1.88, 2.10 and 2.10 (4s, 4X3H, 4xOAc), 2.28 and 2.29 (2s, 2X3H, 2X$COCH_3$), 2.45 (m, 2X3H, 2XCH_aCHO), 2.94 (m, 2H, 2XCH_eCHO), 3.79, 3.81 and 3.83 (3s, 4X3H, 4XOCH_3), 4.34 (q, 1H, J=6.53Hz, H-5'), 4.62 (m, 3H, 2XH-3 and H-5'), 5.14 (m, 4H, 2xH-3' and 2XH-4'), 5.54 and 5.61 (2 broad s, 2H, 2XH-1'), 5.97 and 6.16 (2s, 2H,H-1), 6.88 (m, 2X2H, 2XAr-H).

Step 2: (1'S,1S,3R) and (1'S,1R,3S)-5,8-dimethoxy-3-aceto-1-(2',6'-dideoxy-L-lyxohexopyranose) isochroman

The same procedure described in step 3, example 61, was applied to the products from step 1 herein. Flash chromatography of the crude (Toluene:Ethyl acetate; 6:4) gave 39% yield of non-separable titled diastereoisomers (1:1).

PMR (acetone-d_6, 250 MHz)δ: 1.16 and 1.25 (2d, 2X3H, J=6.6Hz, 2XCH_3-6'), 1.80 (m, 4H, 4XH-2'), 2.24 (s, 2X3H, 2X$COCH_3$), 2.45 (unresolved dd, 2H, CH_aCHO), 2.87 (dd, 2H, CH_eCHO), 3.37 (s, 1H, H-3'), 3.56 (m, 3H, H-3' and 2XH-4'), 3.75 (s, 3X3H, 3xOCH_3), 3.77 (s, 3H, OCH_3), 4.00 and 4.34 (2d, 2H, J=6.6Hz, 2XH-5'), 4.54 (2 unresolved dd, 2H, H-3), 5.35 and 5.41 (2 broad s, 2H, 2XH-1'), 5.89 and 6.10 (2s, 2H, 2XH-1), 6.83 (2X2d, 4H, Ar-H).

Step 3: (1'S,1S,3R) and (1'S,1R,3S)-5,8-dioxo-3-aceto-1-(2',6'-dideoxy-L-lyxohexopyranose)-5,8-dihydroisochroman

The titled products were obtained following CAN oxidation of the products from step 2 herein.

PMR ($CDCl_3$, 250 MHz) δ: 1.29 and 1.42 (2d, 2X2H, J=6.6Hz, 2XCH_3-6'), 1.70 (m, 4H, 4XOH), 1.89 (m, 4H, 4XH-2'), 2.30 and 2.31 (2s, 2X3H, 2X$COCH_3$), 2.43 (2 overlapping dd, 2H, 2XCH_aCHO), 2.89 (2 overlapping dd, 2H, 2XCH_eCHO), 3.65 and 3.70 (2 broad s, 2H, 2XH-4'), 3.90 (m, 2H, 2XH-3'), 3.99 (unresolved q, 1H, H-5'), 4.36 (q, 1H, J=6.8Hz, H-5'), 4.43 (2 overlapping, 2H, 2XH-3), 5.41 and 5.49 (2 broad s, 2H, 2XH-1'), 5.81 and 5.98 (2s, 2H, 2xH-1), 6.79 (2X2d, 4H, Ar-H).

Step 4: (1'S,1S,3R) and (1'S,1R,3S)-methyl-(1-[dideoxy-2',6'-dihydroxy-3',4'-L-lyxohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-c]-pyran-3-yl) ketone (BCH-2117)

The titled compounds were obtained in 43% yield by following the procedure described in step 2, example 5, and using the products from step 3 herein. Flash chromatography (Toluene:Ethyl acetate; 4:6) and final purification by preparative TLC (same solvent conditions) was required.

PMR (DMSO-d_6, 250 MHz) δ: 1.10 and 1.23 (2d, 2X3H, J=6.3Hz, 2XCH_3-6'), 1.54 and 1.87 (2m, 2X2H, 2X2H-2'), 2.25 (s, 6H, 2X$COCH_3$), 2.46 (m, 2H, 2XCH_aCHO), 2.86 (2 overlapping dd, 2H, CH_eCHO), 3.73 (m, 2H, 2XH-3'), 3.89 (q, 1H, J=6.5Hz, H-5'), 4.28 (q, 1H, J=6.3Hz, H-5'), 4.38 (broad s, 1H, H-4'), 4.52 (2X unresolved dd, 2H, 2XH-3), 4.54 (broad s, 1H, H-4'),

5.11 (m, 2H, 2XOH), 5.31 and 5.38 (2 broad s, 2H, 2XH-1'), 5.49 (m, 2H, 2XOH), 5.86 and 5.94 (2s, 2H, 2XH-1), 8.32 and 9.58 (2m, 8H, Ar-H).

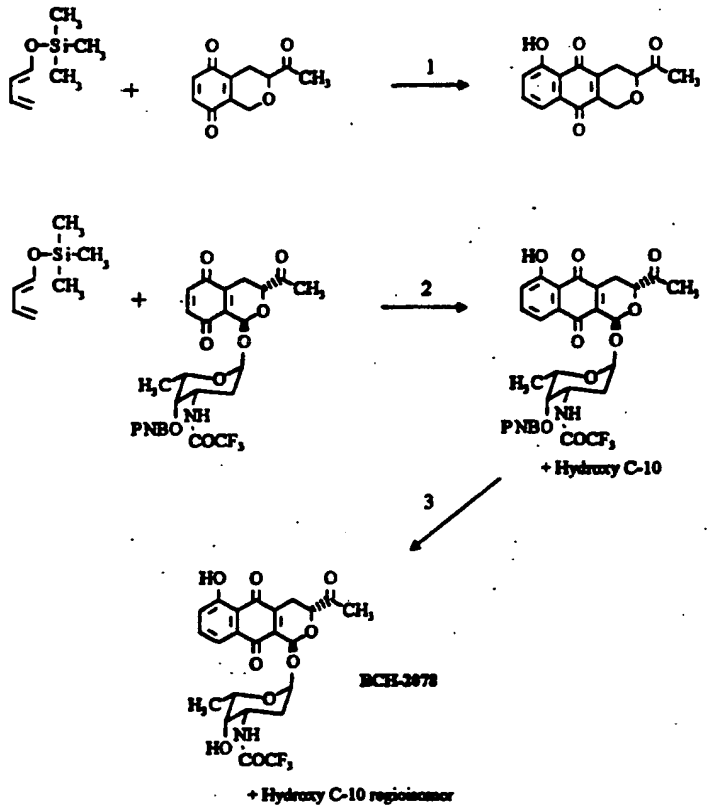
Step 5: (1'S,1S,3R) and (1'S,1R,3S)-5,8-dioxo-3-aceto-1-(2',6'-dideoxy-3',4'-diacetoxy-L-lyxohexopyranose) isochroman

The titled compounds were obtained following CAN oxidation of the products obtained from step 1 herein.
PMR ($CDCL_3$, 250 MHz) δ: 1.10 and 1.22 (2d, 2X3H, J=6.5Hz, $2XCH_3$-6'), 1.93 (large m, 2X2H, 2X2H-2'), 1.92, 1.96, 2.11 and 2.12 (4s, 4X3H, 4XOAc), 2.23 and 2.25 (2s, 2X3H, $2XCOCH_3$), 2.39 (2 overlapping dd, 2H, $2XCH_aCHO$), 2.80 (2 overlapping dd, 2H, $2XCH_eCHO$), 4.10 (q, 1H, J=6.5Hz, H-5'), 4.40 (m, 3H, 2XH-3 and H-5'), 5.10 (m, 4H, 2XH-3', and 2XH-4'), 5.44 and 5.50 (2 broad s, 2H, 2XH-1'), 5.76 and 5.94 (2s, 2H, 2XH-1), 6.57 (2X2d, 4H, Ar-H).

Step 6: (1'S,1S,3R) and (1'S,1R,3S)-methyl-(1-[dideoxy-2',6'-diacetoxy-3',4'-L-lyxohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-c]-pyran-3-yl) ketone (BCH-2118)

The titled compounds were obtained in 51% yield by following the procedure described in step 2, example 5, and using the products from step 5 herein. Aromatization by flash chromatography (Toluene:Ethyl acetate; 8:2). Final purification by preparative TLC (same solvent conditions).
PMR ($CDCl_3$, 250 MHz) δ: 1.17 and 1.33 (2d, 2X3H, J=6.6Hz, $2XCH_3$-6'), 1.88 (m, 2H, 2XH-2'), 1.96 (s, 2X3H, 2XOAc), 2.16 (large m, 2H, 2XH-2'), 2.18 and 2.19 (2s, 2X3H, 2XOAc), 2.32 and 2.34 (2s, 2X3H, $2XCOCH_3$), 2.54 (2X overlapping dd, 2H, $2XCH_aCHO$), 3.07 (2X overlapping dd, 2H, $2XCH_eCHO$), 4.17 (q, 1H, J=6.7Hz, H-5'), 4.51 (2X aoverlapping dd, 2H, 2X H-3), 4.63 (q, 1H, J=6.4Hz, H-5'), 5.19 (m, 4H, 2XH-3'; and 2XH-4'), 5.55 and 5.67 (2 broad s, 2H, 2XH-1'), 6.00 and 6.18 (2s, 2H, 2XH-1), 7.76 and 8.10 (2m, 8H, Ar-H).

Example 66: Phenolic pyranylnaphthoquinone glycosides



Step 1: **Methyl-(6-hydroxy-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-c]-pyran-3-yl) ketone and methyl-(9-hydroxy-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-c]-pyran-3-yl) ketone (BCH-2062)**

The titled compounds were obtained by following the procedure described in step 2 herein and using 1-acetoxybutadiene and 3-acetoisochroman-5,8-dione.

PMR ($CDCl_3$, 250 MHz) δ: 2.33 (2s, 2X3H, $COCF_3$), 2.56 (m, 2H, CH_aCHO), 3.00 (m, 2H, CH_eCHO), 4.07 (dd, 2H, J=10.1Hz and 3.9Hz, H-3), 4.60 (m, 2H, H-1), 4.95 (m, 2H, H-1), 7.26 (m, 2H, Ar-H), 7.62 (m, 2X2H, Ar-H), 11.84 and 11.96 (2s, 2H, OH-5 and OH-8).

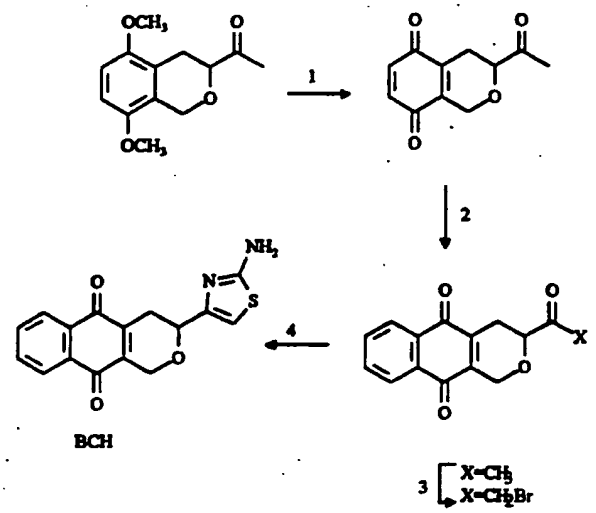
Step 2: **(1'S,1S,3R)-methyl-(6 and 9-hydroxy-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran-3-yl) ketone**

To a mixture of (1'S,1S,3R) glycoside from step 1, example 5, (200 mg, 0.335 mmol) in dry toluene (2.5 ml) under argon atmosphere, was added dropwise the 1-trimethylsilyloxy-1,3-butadiene. After stirring for 18 hours at room temperature, the solvent was removed in vacuo. The residue was dried over vacuum for 10 minutes, dissolved in 5 ml of THF and cooled to 0C. Addition of HCl 1N (5 ml) gave after 30 minutes stirring a complete cleavage of the silyl group. Extractions were done with CH_2Cl_2 (3x30 ml) and the combined organic layers were dried with Na_2SO_4 and then evaporated. The residue was dissolved with 10 ml of dry CH_2Cl_2, at room temperature and under argon, and treated with 200 mg of PCC. After 30 minutes stirring, the reaction mixture was dropped on SiO_2 and flash chromatographed (Toluene:Ethyl acetate; 8:2) to give 162 mg (72% yield) of a non-separable titled regioisomers (1:1).
PMR ($CDCl_3$, 250 MHz) δ: 1.36 and 1.37 (2d, 2X3H, J=6.4Hz, CH_3-6'), 2.14 (2X m, 2X2H, H-2'), 2.34 and 2.35 (2s, 2X3H, $COCH_3$), 2.57 (dd, 2X1H, J=20.1Hz and 11.8Hz, CH_aCHO), 3.09 (dd, 2X1H, J=19.9Hz and 4.1Hz, CH_eCHO), 4.53 (2X unresolved dd, 2X1H, H-3), 4.61 (2Xm, 2X1H, H-3'), 4.77 (2X unresolved q, 2X1H, H-5'), 5.45 (broad s, 2X1H, H-4'), 5.63 (broad s, 2XH, H-1'), 6.19 and 6.21 (2s, 2H, H-1), 6.46 (broad s, 2H, $NHCOCF_3$), 7.32 (m, 2H, Ar-H), 7.67 (m, 2X2H, Ar-H), 8.32 (m, 2X2H, Ar-H), 11.89 and 11.90 (2s, 2H, OH-5 and OH-8).

Step 3: (1'S,1S,3R)-methyl-(6 and 9-hydroxy-1-[2',3',6'-trideoxy-3'-trifluoroacetamido-4'-hydroxy-L-lyxohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-c]-pyran-3-yl-ketone (BCH-2078)

Hydrolysis of the glycosides from step 2 herein with catalytic sodium methoxide in methanol yielded the titled compounds. Flash chromatography (Toluene:Ethyl acetate:acetone; 6:4:2) of the crude gave 83% yield of pure titled regioisomers mixture (1:1).
PMR ($CDCl_3$, 250 MHz) δ: 1.40 and 1.42 (2Xd, 2X3H, J=6.4Hz, CH_3-6'), 1.91 (m, 2X2H, H-2'), 2.31 and 2.32 (2Xs, 2X3H, $COCH_3$), 2.56 (dd, 2X1H, J=19.7Hz and 11.4Hz, CH_aCHO), 3.08 (dd, 2H, J=19.9Hz and 4.2Hz, CH_eCHO), 3.67 (broad d, 2H, H-4'), 4.33 (m, 2H, H-3'), 4.53 (m, 4H, H-3 and H-5'), 5.44 and 5.45 (2s, 2H, H-1'), 6.13 and 6.15 (2S, 2H, H-1), 6.74 (broad d, 2H, $NHCOCF_3$), 7.30 (m, 2H, Ar-H), 7.65 (m, 2X2H, Ar-H), 11.89 and 11.91 (2s, 2H, OH-5 and OH-8).

Example 67: 3-(3'-aminothiazolyl)-5,10-dioxo-1,3,4,5,10-pentahydro-naphtho-[2,3-c]-pyran (BCH)



Step 1: 3-aceto-5,8-dioxo-3,4,5,8-tetrahydro-1H-benzo-[2,3-c]-pyran

CAN oxidation of 5,8-Dimethoxy-3-acetoisochroman yielded the titled compound.

^{1}H NMR ($CDCl_3$, 250 MHz, Bruker) δ: 2.23 (3H, s, $COCH_3$), 2.36 (1H, dd tr, J=17.8Hz, 11.0Hz, 2.9Hz, 4-HCH_a), 2.75 (1H, d tr, J=17.8Hz, 2.9Hz, 4-HCH_e), 3.96 (1H, dd, J=11Hz, 5.3Hz, 3-CH), 4.41 (1H, d tr, J=17.8Hz, 3.5Hz, 1-HCH_a), 4.72 (1H, d tr, J=17.5Hz, 1Hz, 1-HCH_e), 6.71 (2H, m, ArH).

Step 2: 3-aceto-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran

The titled compound was obtained by following the procedure described in step 2, example 5, and using the product from step 1 herein.

^{1}H NMR: ($CDCl_3$, 250 MHz, Bruker) δ: 2.30 (3H, s, $COCH_3$), 2.56 (1H, dd tr, J=18Hz, 11.2Hz, 2.9Hz, 4-HCH_a), 3.01 (1H, d, J=18.0Hz, 4-HCH_e), 4.05 (1H, dd, J=11.2Hz, 3.8Hz, 3-CH), 4.60 (1H, d tr, J=17.8Hz, 4.1Hz, 1-HCHa), 4.95 (1H, d m, J=17.8Hz, 1-HCH_e), 7.73 (2H, m, 7, 8-ArH), 8.08 (2H, m, ArH).

Step 3: 3-bromoacetyl-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran

The titled compound was obtained by following the procedure described in step 1, example 7, and using the product from step 2 herein. ^1H NMR ($CDCl_3$, 250 MHz, Bruker) δ: 2.57 (1H, dd tr, J=18.8Hz, 11.2Hz, 3Hz, 4-HCH_a), 3.02 (1H, d m, J=18.8Hz, 4-HCH_e), 4.21 (1H, d, J=12.9Hz, CHBr), 4.30 (1H, d, J=12.9Hz, CHBr), 4.34 (1H, dd, J=11.2Hz, 4.7Hz, 3-CH), 4.58 (1H, d tr, J=18.0Hz, 3.0Hz, 1-HCH_a), 4.90 (1H, d m, J=18.0Hz, 1-HCH_e), 7.70 (2H, m, 7, 8-ArH), 8.04 (2H, m, 6, 9-ArH).

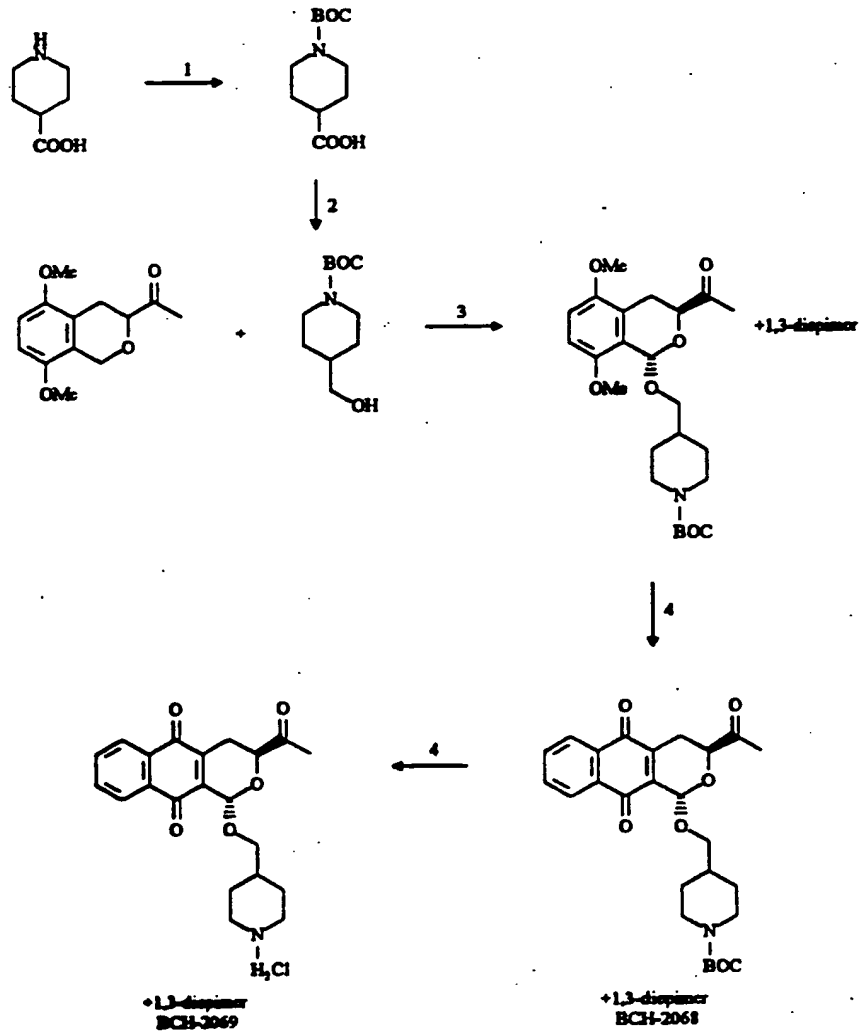
Step 4: 3-(3'-aminothiazolyl)-5,10-dioxo-1,3,4,5,10-pentahydro-naphtho-[2,3-c]-pyran

Bromomethyl ketone from step 3 herein (270 mg, 0.81 mmol) was stirred with thiourea (60 mg, 0.88 mmol) in ether (80 ml) and methylene chloride (10 ml) at room temperature for 4 hours. Three pellets of molecular sieves were used to take up water. Solvent was evaporated to give a white solid. The crude product was washed with chloroform/ether (8:1) first, then basified with potassium carbonate. It was extracted with chloroform. The organic phase was evaporated to give a crude product which was chromatographed to give desired titled product.

dec. 130°C.

^1H NMR ($CDCl_3$, 250 MHz, Bruker), 2.80 (1H, m, 4-HCH_a), 3.09 (1H, br d, J = 18.2 Hz, 4-HCH_e), 4.58 (1H, dd, J = 10.0 Hz, 3.5 Hz, 3-CH), 4.68 (1H, d tr, J = 18.8, 2.9 Hz, 1-HCH_a), 4.95 (1H, dd, J = 18.8 Hz, 2.3 Hz, 1-HCH_e), 5.54 (1H, br s, NH), 6.54 (1H, s, thia-H), 7.73 (1H, m, ArH), 8.08 (1H, m, ArH).

Example 68: Cyclic amine substituted naphthoquinone derivative



Step 1: N-BOC-isonipecotic acid

The titled compound was obtained following standard conditions. ^1H NMR ($CDCl_3$): δ 4.02 (m, 2H, CH_2N), 2.73 (m, 2H, CH_2N), 2.50 (m, 1H, $\underline{C}HCOOH$), 1.91 (m, 2H, $\underline{CH_2}CHCOOH$), 1.64 (m, 2H, $\underline{CH_2}CHCOOH$).

Step 2: N-BOC-4-piperidinemethanol

To a solution of the acid from step 1 (0.11 g, 0.48 mmol) in dry THF (4.8 ml), under argon, at 0°C, was added dropwise BH_3-THF 1.0 M/THF (0.72 ml, 1.5 eq). The solution was stirred at 0°C for 30 minutes and at room temperature for 15 hours. Methanol (10 ml) was then carefully

added to destroy the excess BH_3 and the solvents were evaporated. The residue was poured in CH_2Cl_2/sat. aq. $NaHCO_3$ and the phases were separated. The aqueous layer was extracted with CH_2Cl_2 (2x) and the combined organic extracts were dried over $MgSO_4$. The solids were filtered and the solvent evaporated to give the titled alcohol as a clear oil (0.092 g, 89%).

^1H NMR ($CDCl_3$): δ 4.09 (m, 2H, CH_2N), 3.44 (d, 2H, $\underline{CH_2}OH$), 2.67 (m, 2H, CH_2N), 2.08 (bs, 1H, OH), 1.73-1.52 (m, 2H, $\underline{CH_2}-CH_2N$), 1.48 (s, 9H, BOC), 1.22-1.01 (m, 2H, $\underline{CH_2}-CH_2N$).

Step 3: 1-O-[N-BOC-4-piperidinemethanol]-3-acetyl-5,8-dimethoxy isochroman racemic

The titled compound was obtained via DDQ induced coupling of the alcohol from step 2 herein with 3-aceto-5,8-dimethoxy isochroman. Purification: flash chromatography (silica gel, 2:1 Hex/EtOAc).

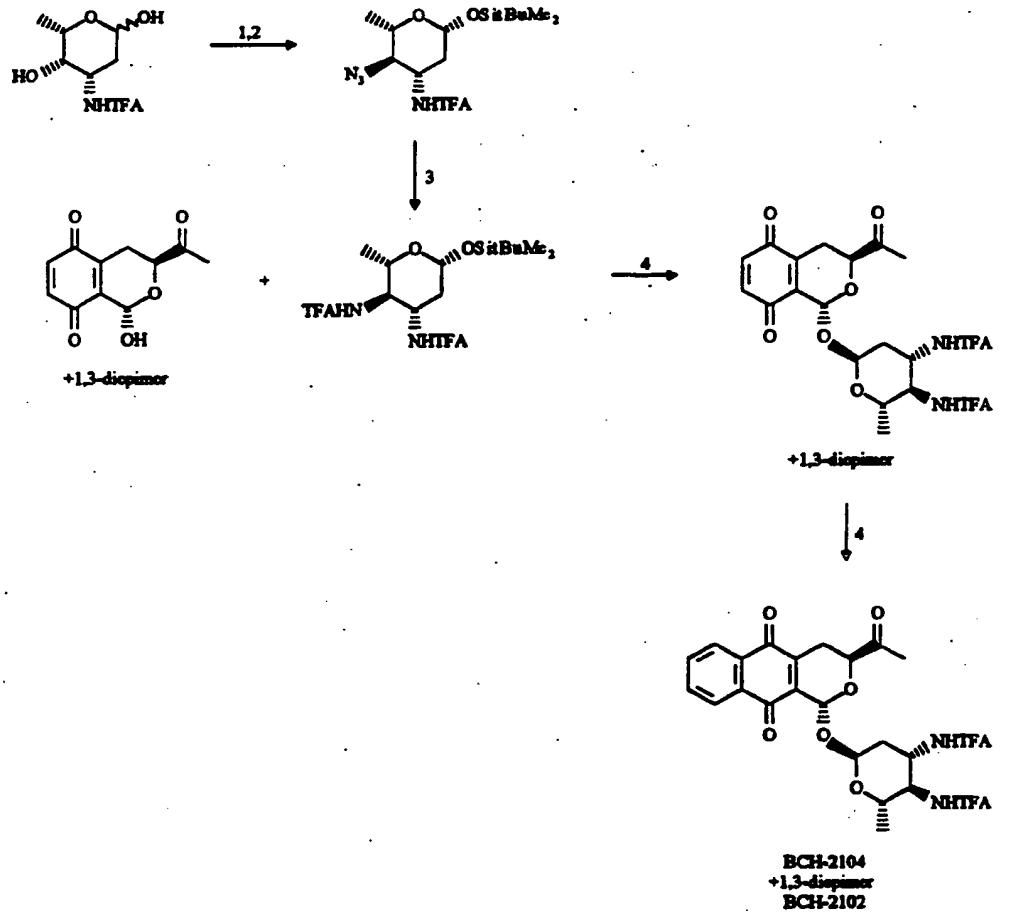
^1H NMR ($CDCl_3$): δ 6.76 (d, 1H, J = 8.8, ArH), 6.70 (d, 1H, J = 8.8, ArH), 5.77 (s, 1H, H-1), 4.59 (dd, 1H, J = 4.2, 12.2, H-3), 4.08 (m, 2H, CH_2N), 3.78 (s, 3H, ArOMe), 3.77 (s, 3H, ArOMe), 3.72 (dd, 1H, J = 6.4, 9.7, H-1'), 3.57 (dd, 1H, J = 6.4, 9.7, H-1'), 3.04 (dd, 1H, J = 4.2, 17.6, H-4), 2.70 (m, 2H, CH_2N), 2.53 (dd, 1H, J = 12.2, 17.6, H-4), 2.33 (s, 3H, $COCH_3$), 1.76 (m, 3H, $\underline{CH_2}\underline{CH}-CH_2O$), 1.21 (m, 2H, $\underline{CH_2}CHCH_2O$).

Step 4: Methyl-(1-O-[2'-piperidinemethanol]-5,10-dioxo-3,4,5,10-tetrahydronaphthaleno-[2,3-c] pyran-3-yl) ketone, racemic, hydrochloride (BCH-2069)

The titled compound was obtained from the precursor from step 3 herein as per previously described procedure.

^1H NMR (DMSO): δ 8.05-7.80 (m, 4H, ArH), 5.69 (s, 1H, H-1), 4.48 (m, 1H, H-3), 3.88 (m, 4H, CH_2N and NH_2Cl), 3.74 (m, 1H, H-1'), 3.60 (m, 1H, H-1'), 3.25 (m, 1H, H-4+H_2O), 2.82 (m, 3H, CH_2N and H-4), 2.31 (s, 3H, $COCH_3$), 2.01-1.70 (m, 3H, $\underline{CH_2}\underline{CH}-CH_2O$), 1.57-1.38 (m, 2H, $\underline{CH_2}CHCH_2O$).

Example 69 Diamino-sugar substituted naphthoquinone derivative



Step 1: (2R,4S,5S,6S)-2-tert-butyldimethylsilyloxy-4-trifluoroacetamido-5-hydroxy-6-methyl-tetrahydropyran

To a solution of the hemiacetal (0.51 g, 2.08 mmol) in dry CH_2Cl_2 (20 ml), under argon, at room temperature, were added successively imidazole (0.28 g, 2 eq) and t-$BuMe_2SiCl$ (0.34 g, 1.1 eq). The solution was stirred at room temperature for 15 hours after which it was poured in sat. aq. $NaHCO_3$. The phases were separated and the aqueous layer was extracted with CH_2Cl_2 (2x). The combined organic extracts were dried over $MgSO_4$, the solids were filtered and the solvent evaporated to give 0.72 g (97%) of the titled silyloxy-sugar as a white solid.

^1H NMR ($CDCl_3$): δ 6.82 (bd, 1H, NH), 4.78 (dd, 1H, J = 2.2, 9.2, H-1), 4.09 (m, 1H, H-3), 3.62 (q, 1H, J = 6.6, H-5), 3.48 (d, 1H, J = 2.6, H-4), 2.44 (bs, 1H, OH), 2.08 (dd, 1H, J = 5.0, 13.0, H-2), 1.55 (ddd, 1H, J = 9.2, 13.0, 13.0, H-2), 1.29 (d, 3H, J = 6.6, H-6), 0.89 (s, 9H, t-Bu), 0.12 (s, 3H, SiMe), 0.11 (s, 3H, SiMe).

Step 2: (2R,4S,5R,6S)-2-tert-butyldimethylsilyloxy-4-trifluoroacetamido-5-azido-6-methyl-tetrahydropyran

To a solution of the alcohol (0.40 g, 1.11 mmol) in dry CH_2Cl_2 (11.1 ml), under argon, at -30°C were added successively pyridine (0.45 ml, 5 eq) and Tf_2O (0.37 ml, 2 eq) and the solution was stirred at -10°C for 1 hour. It was then poured in sat. aq. $NaHCO_3$ and the phases were separated. The aqueous layer was extracted with CH_2Cl_2 (2x) and the combined organic extracts were dried over $MgSO_4$. The solids were filtered and the solvents were evaporated to dryness. The red oil obtained was dissolved in dry DMF (11.1 ml), under argon, at room temperature, and NaN_3 (0.36 g, 5 eq) was added. The suspension was stirred for 5 hours after which it was poured in EtOAc. This organic phase was washed with water (3x) and brine. It was then dried over $MgSO_4$, the solids were filtered and the solvent evaporated to give the titled azido-trifluoroacetamide as a clear oil (0.27 g, 68%).
^1H NMR ($CDCl_3$): δ 6.44 (bd, 1H, J = 8.6, NH), 4.82 (dd, 1H, J = 2.1, 8.8, H-1), 4.09 (ddd, 1H, J = 4.7, 9.7, 12.8, H-3), 3.41 (dq, 1H, J = 6.1, 9.2, H-5), 2.97 (dd, 1H, J = 9.7, 9.7, H-4), 2.21 (ddd, 1H, J = 2.1, 4.7, 12.8, H-2), 1.67 (ddd, 1H, J = 8.8, 12.8, 12.8, H-2), 1.39 (d, 3H, J = 6.1, H-6), 0.89 (s, 9H, tBu), 0.12 (s, 3H, SiMe), 0.10 (s, 3H, SiMe).

Step 3: (2R,4S,5R,6S)-2-tert-butyldimethylsilyloxy-4,5-bis-trifluoroacetamido-6-methyl-tetrahydro-pyran

The azido saccharide from step 2 was reduced as per standard contiditons. Purification: flash chromatography (silica gel, 85:15 Hexanes/EtOAc).
^1H NMR ($CDCl_3$): δ 7.85 (bd, 1H, J = 9.4, NH), 7.48 (bd, 1H, J = 9.7, NH), 4.84 (d, 1H, J = 7.8, H-1), 4.38 (m, 1H, H-3), 3.96 (m, 1H, H-4), 3.56 (dq, 1H, J = 6.1, 9.6, H-5), 2.19 (m, 1H, H-2), 1.78 (m, 1H, H-2), 1.29 (d, 3H, J = 6.1, H-6), 0.89 (s, 9H, t-Bu), 0.12 (s, 3H, SiMe), 0.11 (s, 3H, SiMe).

Step 4: (1R,3S,1'S) and (1S,3R,1'S)-Methyl-(1-[2',3',4',6'-tetradeoxy-3',4'-bis-trifluoroacetamido-L-arabinohexopyranose]-5,10-dioxo-3,4,5,10-

tetrahydronaphthaleno-[2,3-c] pyran-3-yl) ketone (BCH-2104 and BCH-2102)

To a solution of the hydroxyquinone (72 mg, 0.33 mmole) and di-trifluoroacetamido sugar from step 3 herein (162 mg, 1.1 eq) in 6.5 mL of a 9:1 mixture of anhydrous CH_2Cl_2/Acetone, under argon, at -30 °C, were added activated 4A M.S. (200 mg) and TMSOTf (94 mL). The solution was stirred at -30 °C for 4 hr and 5% $NaHCO_3$ (5mL) was added. The biphasic solution was stirred for 15 min while the temperature was allowed to go back to r.t. It was then filtered through Celite and poured in water. The phases were separated and the aqueous layer was extracted with CH_2Cl_2 (2x). The combined organic extracts were dried over $MgSO_4$, The solids were filtered and the solvants evaporated. The pale brown solid obtained was dissolved in dry toluene (6.5 mL) and 1-acetoxybutadiene (0.19 mL, 5 eq) was added. The solution was stirred at r.t. , under argon for 15 hr. Silica gel was added and air was bubbled through the solution. This suspension was then placed on top of a silica gel column and the column was eluted with hexanes (1 reservoir). When the hexanes was all gone , it was replaced with 2:1 hexanes/ethyl acetate and themixture of isomers was collected. This mixture was further purified by chromatography (10% acetone/toluene) to give 58 mg (30%) of the titled separated isomers.

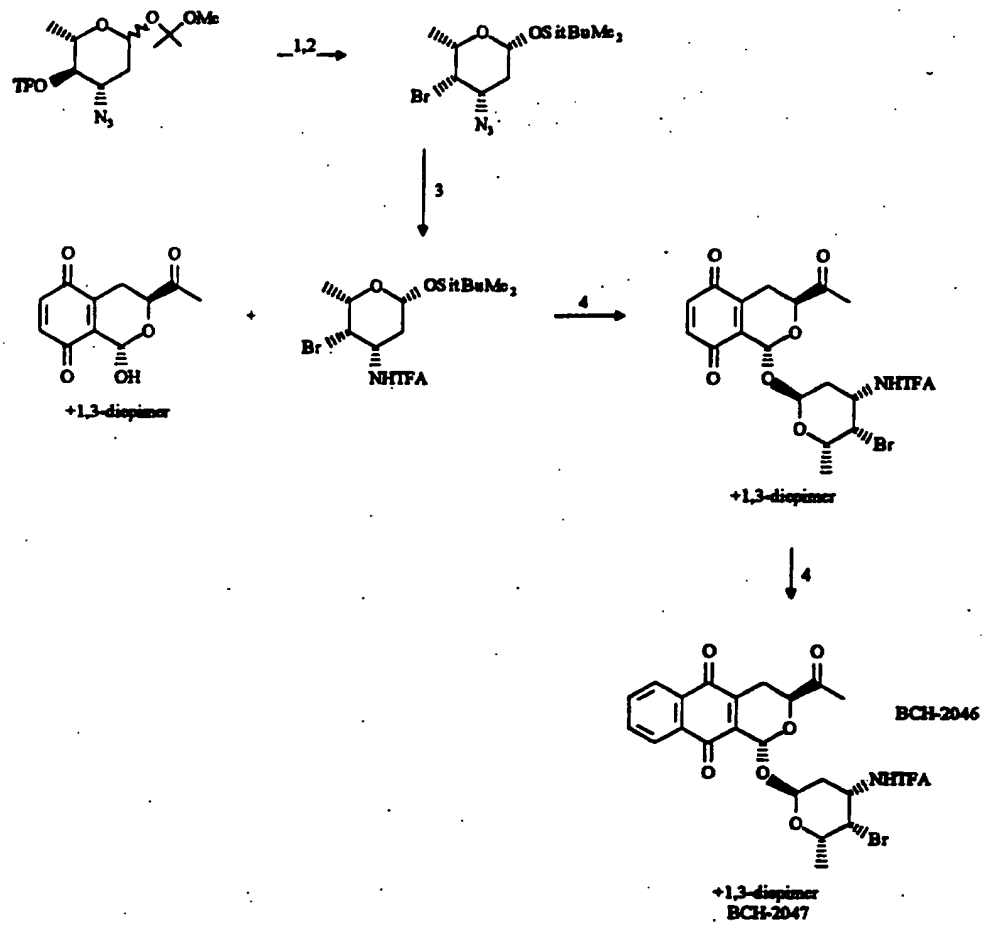
The faster running fraction had: 33 mg, m.p.: 180-195 °C dec.

^1H NMR (Acetone-d_6) : d 8.47 (d, 1H, J= 9.1, NH), 8.36 (d, 1H, J= 9.4, NH), 8.11-8.04 (m, 2H, ArH), 7.92-7.85 (m, 2H, ArH), 6.03 (s, 1H, H-1), 5.65 (s, 1H, H-1'), 4.68 (dd, 1H, J= 4.1, 11.6, H-3), 4.58-4.36 (m, 2H, H-3' and H-4'), 3.85 (q, 1H, J= 10.1, H-5'), 3.02 (dd, 1H, J= 4.1, 19.6, H-4), 2.51 (dd, 1H, J= 11.6, 19.6, H-4), 2.32 (s, 3H, COMe), 2.28-2.09 (m, 2H, H-2'), 1.28 (d, 3H, J= 6.3, H-6').

The slower running fraction had: 25 mg, m.p.: 143-153 dec.

^1H NMR ($CDCl_3$) : d 8.55 (d, 1H, J= 9.2, NH), 8.46 (d, 1H, J= 9.1, NH), 8.13-8.07 (m, 2H, ArH), 7.95-7.88 (m, 2H, ArH), 6.17 (s, 1H, H-1), 5.63 (t, 1H, J= 2.5, H-1'), 4.71 (dd, 1H, J= 4.3, 11.6, H-3), 4.61-4.34 (m, 2H, H-3' and H-4'), 3.86 (q, 1H, J= 10.2, H-5'), 2.99 (dd, 1H, J= 4.3, 19.7, H-4), 2.58 (dd, 1H, J= 11.6, 19.7, H-4), 2.32 (s, 3H, COMe), 2.28-2.13 (m, 2H, H-2'), 1.37 (d, 3H, J= 6.2, H-6').

Example 70: 4'-iododaunosamine substituted naphtoquinone derivative



Step 1: **(2S,4S,5S,6S)-2-(2'-methoxy-2'-propanoxy)-4-azido-5-bromo-6-methyl-tetrahydropyran**

To a solution of the triflate (1.06 g, 2.80 mmol) in a 1:1 mixture of CH_2Cl_2/toluene (15 ml), under argon, at room temperature, was added nBu_4NBr (1.34 g, 1.5 eq) and the solution was stirred for 3 hours. It was then poured in sat. aq. $NaHCO_3$ and the phases were separated. The aqueous layer was extracted with CH_2Cl_2 (2x) and the combined organic extracts were dried over $MgSO_4$. The solids were filtered and the solvents evaporated to give a crude oil that was purified by flash chromatogrphy (silica gel, 85:15 Hexanes/EtOAc). The titled bromo-azide was obtained in 66% yield (0.57 g).

^1H NMR ($CDCl_3$): δ 5.34 (d, 1H, J = 3.4, H-1), 4.27 (s, 1H, H-4), 4.02 (q, 1H, J = 6.2, H-5), 3.96 (m, 1H, H-3), 3.20 (s, 3H, OMe), 2.23 (ddd, 1H, J = 3.4, 12.5, 12.5, H-2), 1.74 (dd, 1H, J = 4.26, 12.5, H-2), 1.40

(s, 3H, gemdimethyl), 1.35 (s, 3H, gemdimethyl), 1.25 (d, 3H, J = 6.2, H-6).

Step 2: (2R,4S,5S,6S)-2-tert-butyldimethylsilyloxy-4-azido-5-bromo-6-methyl-tetrahydropyran

To a solution of the bromo-azide from step 1 (0.57 g, 1.84 mmol) in dry CH_2Cl_2 (9.0 ml), under argon, at 0°C, was added slowly CF_3COOH (7 µl, 0.05 eq) and the solution was stirred for 60 minutes. The solvent and reagent were then evaporated to dryness and the crude hemiacetal was dissolved in a dry mixture (15:1) of CH_2Cl_2/DMF (9.2 ml). Imidazole (0.25 g, 2 eq) was then added followed by t-BuMe_2SiCl (0.31 g, 1.1 eq). The solution was stirred at room temperature for 15 hours after which it was poured in sat. aq. $NaHCO_3$. The phases were separated, the aqueous layer was extracted with CH_2Cl_2 (2x) and the combined organic extracts were dried over $MgSO_4$. The solids were filtered and the solvent evaporated to give the titled TBDMS protected bromo-azide (0.30 g, 46%) as a clear oil.

^1H NMR ($CDCl_3$): δ 4.80 (dd, 1H, J = 2.5, 8.7, H-1), 4.15 (dd, 1H, J = 1.2, 3.3, H-4), 3.57 (ddd, 1H, J = 3.3, 4.4, 11.8, H-3), 3.44 (dq, 1H, J = 1.2, 6.1, H-5), 2.11-1.88 (m, 2H, H-2), 1.33 (d, 3H, J = 6.1, H-6), 0.90 (s, 9H, t-Bu), 0.14 (s, 3H, SiMe), 0.11 (s, 3H, SiMe).

Step 3: (2R,4S,5S,6S)-2-tert-butyldimethylsilyloxy-4-trifluoroacetamido-5-bromo-6-methyl-tetrahydropyran

To a solution of the azide from step 2 herein (0.30 g, 0.84 mmol) in a 19:1 mixture of THF/H_2O (8.4 ml) was added Ph_3P (0.33 g, 1.5 eq) and the solution was heated at 50°C for 3 hours. It was then poured in sat. aq. $NaHCO_3$ and the aqueous phase was extracted with CH_2Cl_2 (3x). The combined organic extracts were dried over $MgSO_4$. The solids were filtered and the solvent evaporated to dryness to give a crude amine that was dissolved in dry CH_2Cl_2 (8.4 ml). To this solution, under argon, at -30°C, were added successively dry pyridine (0.14 ml, 2 eq) and TFA_2O (0.13 ml, 1.1 eq). The solution was stirred for 90 minutes at -30°C and was then poured in sat. aq. $NaHCO_3$. The phases were separated, the aqueous layer was extracted with CH_2Cl_2 (2x) and the combined organic extracts were dried over $MgSO_4$. The solids were

filtered and the solvent was evaporated to give the titled crude bromo-trifluoroacetamide in 72% yield (0.26 g).

^{1}H NMR ($CDCl_3$): δ 6.67 (bd, 1H, J = 7.3, NH), 4.84 (dd, 1H, J = 5.4, 6.5, H-1), 4.28-4.17 (m, 2H, H-3 and H-4), 3.58 (q, 1H, J = 6.1, H-5), 1.89-1.83 (m, 2H, H-2), 1.32 (d, 3H, J = 6.1, H-6), 0.88 (s, 9H, t-Bu), 0.12 (s, 3H, SiMe), 0.10 (s, 3H, SiMe).

Step 4: (1R,3S,1'S)-Methyl-(1-[2',3',4',6'-tetradeoxy-3'-trifluoroacetamido-4'-bromo-L-lyxohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphthaleno-[2,3-c] pyran-3-yl) ketone

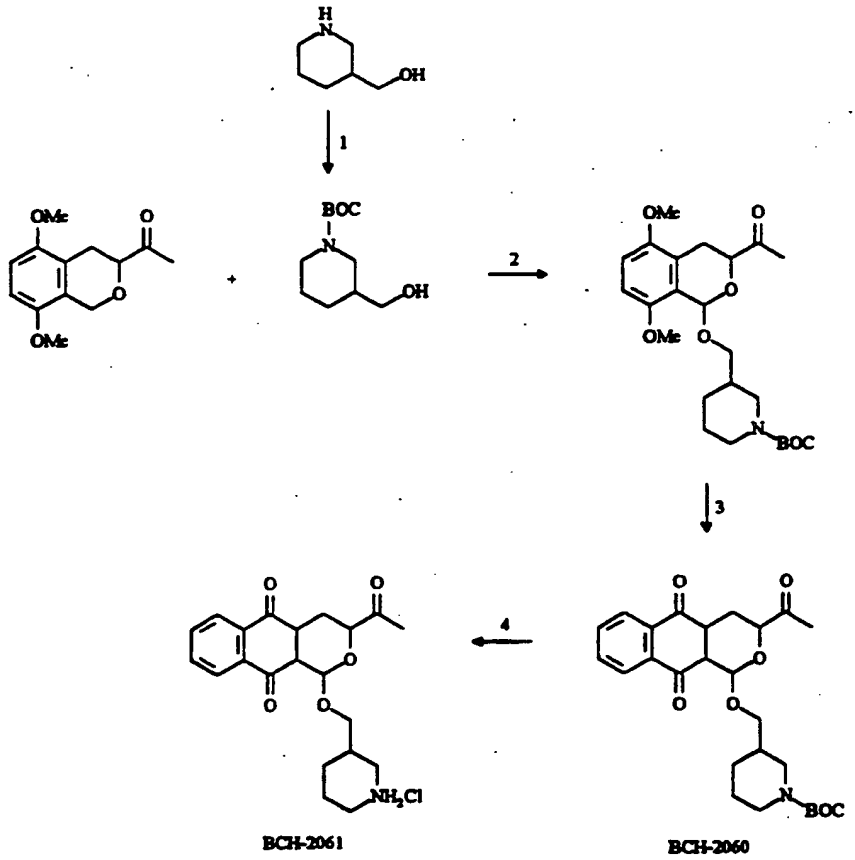
The titled compound was obtained as per previous procedures from the sugar of step 3 and the isochromandione. Purification: flash chromatography (silica gel, toluene/acetone 95:5). The two isomers are separable by chromatography.

^{1}H NMR ($CDCl_3$): δ 8.15-8.07 (m, 2H, ArH), 7.81 -7.76 (m, 2H, ArH), 6.46 (bd, 1H, J = 8.4, NH), 6.01 (s, 1H, H-1), 5.62 (d, 1H, J = 3.2, H-1'), 4.54 (dd, 1H, J = 4.0, 11.7, H-3), 4.42 (m, 1H, H-3'), 4.37 (s, 1H, H-4'), 4.11 (q, 1H, J = 6.5, H-5'), 3.11 (dd, 1H, J = 4.0, 19.7, H-4), 2.53 (dd, 1H, J = 11.7, 19.7, H-4), 2.35 (s, 3H, COMe), 2.14 (td, 1H, J = 3.2, 12.9, H-2'), 1.91 (dd, 1H, J = 4.5, 12.9, H-2'), 1.32 (d, 3H, J = 6.5, H-6').

The (1S,3R,1'S)-Methyl-(1-[2',3',4',6'-tetradeoxy-3'-trifluoroacetamido-4'-bromo-L-lyxohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphthaleno-[2,3-c] pyran-3-yl) ketone (BCH-2047) had:

^{1}H NMR ($CDCl_3$): δ 8.15-8.08 (m, 2H, ArH), 7.82-7.74 (m, 2H, ArH), 6.50 (bd, 1H, J = 8.5, NH), 6.18 (s, 1H, H-1), 5.49 (d, 1H, J = 3.4, H-1'), 4.58 (q, 1H, J = 6.4, H-5'), 4.48 (dd, 1H, J = 4.2, 11.6, H-3), 4.40 (s, 1H, H-4'), 4.40 (m, 1H, H-3'), 3.08 (dd, 1H, J = 4.2, 19.7, H-4), 2.57 (dd, 1H, J = 11.6, 19.7, H-4), 2.32 (s, 3H, COMe), 2.18 (td, 1H, J = 3.4, 13.0, H-2'), 1.79 (dd, 1H, J = 4.4, 13.0, H-2'), 1.49 (d, 3H, J = 6.4, H-6').

Example 71: Cyclic amine substituted naphthoquinone derivative



Step 1: N-BOC-3-piperidinemethanol

The titled compound obtained following protection with BOC had:
^{1}H NMR ($CDCl_3$): δ 3.90-3.65 (m, 2H), 3.48 (d, 2H, CH_2OH), 3.25-2.75 (m, 2H), 2.28 (be, 1H, OH), 1.86-1.54 (m, 4H), 1.25 (m, 1H).

Step 2: 1-O-[N-BOC-3-piperidinemethanol]-3-acetyl-5,8-dimethoxy isochroman, mixture of isomers

The titled compound was obtained from the precursor of step 1 herein and 5,8-dimethoxy-3-acetoisochroman as per procedure described earlier.
Purification: flash chromatography (silica gel, 2:1 Hexanes/EtOAc).
The isomers were not separable by flash chromatography.
^{1}H NMR ($CDCl_3$): δ 6.75-6.65 (m, 2H, ArH), 5.74+5.73 (2s, 1H, H-1), 4.60 (m, 1H, H-3), 4.05-3.56 (m, 4H, H-1' and CH_2N), 3.04 (dd, 1H, H-4), 2.86-2.62 (m, 2H, CH_2N), 2.53 (dd, 1H, H-4), 2.33 (s, 3H, $COCH_3$), 1.94-1.79 (m, 2H), 1.68 (m, 1H), 1.48 (s, 9H, BOC), 1.37-1.24 (m,2 H).

Step 3: Methyl-(1-O-[N-BOC-3-piperidinemethanol]-5,6-dioxo-3,4,5,10-tetrahydronaphthaleno-[2,3-c] pyran-3-yl) ketone, mixture of isomers (BCH-2060)

The titled compound was obtained from the product from step 2 herein, following previously described procedures. Purification: flash chromatography (silica gel, 2:1 Hexanes/EtOAc). The isomers were not separable by flash chromatography.

^{1}H NMR ($CDCl_3$): δ 8.12-8.03 (m, 2H, ArH), 7.78-7.67 (m, 2H, ArH), 6.72 (s, 1H, H-1), 4.54 (m, 1H, H-3), 4.10-3.55 (m, 4H, H-1' and CH_2N), 3.04 (dd, 1H, H-4), 2.90-2.60 (m, 2H, CH_2N), 2.51 (dd, 1H, H-4), 2.30 (s, 3H, $COCH_3$), 1.97-1.72 (m, 2H), 1.61 (m, 1H), 1.48 (s, 9H, BOC), 1.34-1.15 (m, 2H).

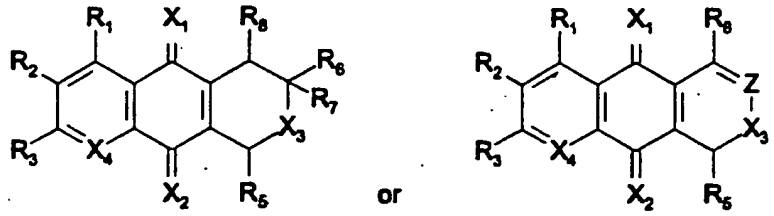
Step 4: Methyl-(1-O-[3-piperidinemethanol]-5,10-dioxo-3,4,5,10-tetrahydronaphthaleno-[2,3-c] pyran-3-yl) ketone hydrochloride salt, mixture of isomers (BCH-2061)

The titled compound was obtained from the tricyclic product from step 3 herein following acidic hydrolysis.

^{1}H NMR (DMSO-d_6): δ 8.23-7.84 (m, 4H, ArH), 5.68+5.67 (2s, 1H, H-1), 4.48 (m, 1H, H-3), 3.83-3.57 (m, 2H, H-1'), 3.29-3.15 (m, 2H, CH_2N), 2.84 (dd, 1H, H-4), 2.66 (m, 2H, CH_2N), 2.43 (m, 1H, H-4), 2.29 (s, 3H, $COCH_3$), 1.74-1.72 (m, 4H), 1.25 (m, 1H).

We claim:

1. A compound of the formula:



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wherein

X_1 and X_2 are independently selected from the group consisting of

O, S, and N(R), wherein R is selected from the group consisting of hydrogen, hydroxyl, C_{1-16} alkyl, C_{1-16} acyl and C_{1-16} alkylamine:

X_3 is selected from the group consisting of O, S, SO, SO_2, and NR, wherein R is selected from the group consisting of hydroxyl:

C_{1-16} acyl, C_{1-16} alkyl, C_{1-16} aryl, C_{1-16} haloacyl, and hydrogen.

X_4 is selected from the group consisting of C-Q, nitrogen, and NO:

R_1, R_2, R_3, and Q are independently selected from the group consisting of hydrogen, hydroxyl, C_{1-16} alkyl, C_{1-16} alkoxyl, C_{3-8} cycloalkyl, tosyl, mesylate, acetate optionally substituted with a C_{1-8} alkyl, triflate, trifluoroacetate, halogen, nitro, cyano, C_{1-16} acyl, C_{1-16} arylacyl, aminoalkylaminoalcohol of formula $NH(CH_2)_nNH(CH_2)_mOH$ wherein n and m are independently 1 to 4, aminoalkylaminoalkylhalide of formula $NH(CH_2)_nNH(CH_2)_mX$ wherein n and m are independently 1 to 4 and X is a halogen, amino, which may be unsubstituted or mono or

di-substituted by C_{1-8} alkyl, C_{3-8} cycloalkyl, C_{1-8} acyl, trifluoroacyl, C_{7-18} aralkyl and C_{6-18} aryl; C_{2-8} alkenyl, and C_{2-8} alkynyl,

haloalkylnitrosoureido of the formula $NH(CO)N(NO)(CH_2)_n CH_2X$, wherein n is 0 to 4 and X is a halogen, and

$-NH(CH_2)n\ N\ R^*\ R^{**}$ wherein n is 1 to 6, R^* and R^{**} are independently selected from hydrogen, C_{1-8} alkyl, C_{6-18} aryl, C_{7-18} aralkyl, C_{1-8} acyl, and trifluoroacyl,

a group of the formula -O-C(R)=O wherein R is selected from the group consisting of hydrogen, C_{1-16} alkyl, C_{3-8} cycloalkyl, C_{2-12} alkoxyalkyl, C_{7-18} aralkyl, C_{7-18} araloxyalkyl, C_{7-18} aryloxyalkyl and C_{6-18} aryl:

Z is one of C-R_6 or C-R_7:

R_6 is selected from the group consisting of C_{1-16} hydroxime, C_{6-18} hydrazone, C_{1-16} hydroxyalkyl, hydrogen, C_{6-18} aryl, C_{7-18} aryloxyalkyl, C_{7-18} araloxyalkyl, phenyl, C_{1-16} alkyl, acetoxy, C_{1-16}

dihydroxyalkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-8} cycloalkyl, squaric acid, C_{1-16} alkyl squarate, amino, cyano, dimethylphosphonato, phenyl sulfone, C_{1-8} aryl sulfone, and

C_{1-8} acetyl, agroup of the formula -C(R) = X* wherein X is selected from the group consisting of two hydrogens, one hydrogen and R* is selected from a C1-8 alkyl, C2-8 alkenyl, C7-18 aralkyl, and O, or its dioxolane or dioxane or dialkoxy C1-8 ketal, and wherein R is selected from the group consisting of hydrogen, C_{1-16} alkyl, C_{1-8} thioalkyl, C_{3-8} cycloalkyl, C_{6-18} aryl, C_{7-18} aralkyl, fluoromethyl, difluoromethyl, C_{1-8} hydroxyalkyl, C_{2-16} alkene, squaric acid, C_{2-16} alkyne, C_{1-8} thioalkyl, C_{6-18} thioaryl, C_{1-4} alkyl squarate, C_{2-8} alkoxyalkyl, C_{6-18} araloxyalkyl, C_{2-18} acyloxyalkyl, C_{1-8} alkoxy, hydroxy, acetoxy methyl, bromomethyl, C_{1-8} aceto, amino which may be unsubstituted or mono- or di-substituted by hydrogen, C_{1-8} alkyl, C_{3-8} cycloalkyl, C_{1-8} acyl, trifluoroacyl, C_{7-18} aralkyl, C_{6-18} aryl,

a group of the formula -CHR* R**, wherein R* and R** are independently selected from the group consisting of C_{1-8} alkyl, hydrogen, PO $(OR)_2$ wherein R is selected from the group consisting of hydrogen, C_{1-8} alkyl, C_{1-8} acyl, C_{6-18} aryl, C_{7-18} aralkyl, and

a group of the formula $-(CH_2)_nZ^*$ wherein n is O to 7 and Z* is from the group consisting of hydrogen, C_{1-8} acyl, C_{6-18} aryl, C_{7-18} aralkyl, pyrolone, and a 5 or 6 membered aromatic or non-aromatic heterocycle containing one or more heteroatoms selected from the group consisting of O, S, N, SO, SO_2, P, PO and NR wherein R is selected from the group consisting of hydrogen, hydroxyl, C_{1-8} acyl, C_{1-4} alkyl and C_{6-12} aryl;

said heterocycle being optionally substituted with one or more halogens, hydroxy, C_{6-18} aryl sulfone, C_{1-16} alkoxy, C_{1-16} alkyl, nitro, C_{1-16} hydroxyalkyl,

amino, which may be unsubstituted or mono- or di-substituted by C_{1-8} alkyl, C_{3-8} cycloalkyl, C_{1-8} acyl, trifluoroacyl, C_{7-18} aralkyl, C_{6-18} aryl, C_{2-8} alkenyl, C_{2-8} alkynyl and hydroxy,

Z* can also be a group of the formula -NR* R** wherein R* and R** are independently selected from the group consisting of hydrogen, C_{1-8} alkyl, C_{1-8} acyl, C_{6-18} aryl, C_{7-18} aralkyl, C_{1-8} haloalkyl, C_{1-8} hydroxyalkyl, C_{1-8} alkoxyalkyl, C_{1-8} acyloxyalkyl, C_{6-12} araloxyalkyl, and a group of formula $-CO(CH_2)_n$ $C(PO(OR)_2)_2$ wherein n is 1 to 4 and R is hydrogen or C_{1-8} alkyl; and a naturally occurring amino acid;

a group of the formula -C(OR)=O, where R is selected from the group consisting of hydrogen, C_{1-16} alkyl, C_{3-8} cycloalkyl, C_{1-8} hydroxyalkyl, C_{1-8} alkoxyalkyl, C_{7-18} aryloxyalkyl, C_{6-18} araloxyalkyl, C_{6-18} aryl and C_{7-18} aralkyl;

a group of the formula $-(CH_2)_n$ C(R)=O, wherein n is 1 to 6 and wherein R is selected from the group consisting of hydrogen, hydroxyl, C_{1-16} alkyl, C_{3-8} cycloalkyl, C_{1-8} hydroxyalkyl, C_{2-8} alkoxyalkyl, C_{1-8} alkoxy, C_{7-18} aryloxyalkyl, C_{7-18} araloxyalkyl, C_{6-18} aryl, C_{7-18} aralkyl,

amino which may be unsubstituted, mono- or di-substituted by C_{1-8} alkyl, C_{3-8} cycloalkyl, acyl, trifluoroacyl, C_{2-12} aralkyl, C_{6-12} aryl, a 5 or 6 membered aromatic or non aromatic heterocycle containing one or more heteroatoms selected from the group consisting of O, S, N, SO, SO_2, P, PO, and NR wherein R is

selected from the group consisting of hydrogen, oxygen, hydroxyl, acyl, C_{1-4} alkyl and aryl,

said heterocycle being optionally substituted with one or more halogens, C_{6-18} arylsulfone, hydroxy, C_{1-16} alkoxy, nitro, C_{1-16} alkyl, C_{1-16} hydroxyalkyl, amino which may be unsubstituted or mono- or disubstituted by C_{1-8} alkyl, C_{3-8} cycloalkyl, acyl, trifluoroacyl, aralkyl or aryl; C_{2-8} alkenyl, C_{2-8} alkynyl and hydroxy:

R_7 is selected from the group consisting of hydrogen, C_{1-16} alkyl, halogen, amino, hydroxy, C_{1-16} alkoxy, thiol, cyano, sulfide, acyl of the formula -C(R)=O wherein R is selected from

the group consisting of hydrogen, C_{1-16} alkyl, C_{1-16} alkoxy, C_{3-8} cycloalkyl, C_{1-8} hydroxyalkyl, C_{7-18} araloxyalkyl, C_{2-8} alkoxyalkyl, C_{2-8} acyloxyalkyl, C_{6-12} aryloxyalkyl, squaric acid or squarate, amino which may be unsubstituted or mono- or di-substituted by C_{1-8} alkyl, C_{3-8} cycloalkyl, C_{1-8} acyl, cyano, trifluoroacyl, C_{7-18} aralkyl or C_{6-12} aryl, and a naturally occuring amino acid;

a group of the formula -C(OR)=O wherein R is selected from the group consisting of hydrogen, C_{1-16} alkyl, C_{3-8} cycloalkyl, C_{1-8} hydroxyalkyl, C_{2-8} alkoxyalkyl, C_{7-12} aryloxyalkyl, C_{7-12} araloxyalkyl, C_{6-12} aryl, C_{7-18} aralkyl and C_{1-16} alkenyl:

R_5 and R_8 are independently selected from the group consisting of hydrogen, halogen, hydroxyl, C_{1-16} alkoxyl, C_{1-16} alkyl, C_{2-16} acetylenyl, a group of the formula $-(CH_2)_n-NR^*R^{**}$ wherein n is 1 to 6, and R* and R** are independently selected from a group consisting of C_{1-8} alkyl, C_{1-4} acyl, C_{3-8} cycloalkyl, hydrogen, C_{2-8} carboalkoxy, C_{2-8} alkene, C_{2-8} alkyne, C_{6-12} aryl, and $(OCH_2CH(PO(OR)_2)_2$

wherein R is a hydrogen or a C_{1-8} alkyl and wherein n is 0 to 5;

C_{3-8} cycloalkyl, C_{2-16} alkenyl, C_{1-16} alkoxyalkylamino, cyano;

a group of the formula -O-C(R)=O, wherein R is selected from the group consisting of hydrogen, C_{1-16} alkyl, C_{3-8} cycloalkyl, C_{2-8} alkoxyalkyl, and C_{6-12} aryl;

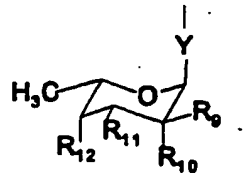
an acyl of the formula -C(R)=O, wherein R is selected from the group consisting of hydrogen, thiol, C_{1-16} thioalkyl, C_{1-16} alkyl, C_{3-8} cycloalkyl, C_{1-8} hydroxyalkyl, C_{2-8} alkoxyalkyl, C_{7-12} araloxyalkyl, C_{2-8} acyloxyalkyl, amino which may be unsubstituted or mono- or di-substituted, and a naturally occurring amino acid or a synthetic amino acid;

a group of the formula -C(OR)=O, wherein R is selected from the group consisting of hydrogen, C_{1-16} alkyl and C_{3-8} cycloalkyl, acosamine, glucosamine, N-chloroethyl-nitrosoureidoglucosamine, 2,6-dideoxyrhamnose, thioglucose, thiodaunosamine, thiol, C_{1-12} thioalkyl, a naturally occuring amino acid or di- and tri-peptides thereof, a group of the formula -Z*-CHRR* wherein Z* is selected from the group consisting of O, CH_2, NR** wherein R** is from the group consisting of hydrogen, C_{1-8} alkyl, C_{2-8} acyl or C_{6-12} aryl,

R and R* are independently selected from the group consisting of hydrogen, C_{1-12} alkyl, C_{6-12} aryl, C_{2-8} dihydroxyalkyl, C_{2-8} alkene, C_{2-8} alkyne, C_{1-8} alkoxy, C_{1-8} alkylamino, C_{3-8} cycloalkyl, C_{2-8} carboalkoxy, a 5 or 6 membered aromatic or non-aromatic heterocycle containing one or more heteroatoms selected from the group consisting of O, S, N, SO, SO_2, P, PO, and NR

wherein R is selected from the group consisting of hydrogen, hydroxyl, C_{1-8} acyl, C_{1-}

4 alkyl and C_{6-12} aryl, said heterocycle being optionally substituted with one or more halogens, hydroxy, C_{6-18} aryl sulfone, cyano C_{1-16} alkoxy, C_{1-16} alkyl, nitro, C_{1-16} hydroxyalkyl, amino, which may be unsubstituted or mono-or di-substituted by C_{1-8} alkyl, C_{3-8} cycloalkyl, C_{1-8} acyl, trifluoroacyl, C_{7-18} aralkyl, C_{6-18} aryl, C_{2-8} alkenyl, C_{2-8} alkynyl and hydroxy; mono or oligosaccharides of the formula:



wherein Y is selected from the group consisting of oxygen, sulfur, sulfoxide, sulfone, CR*R**, wherein R* and R** are independently selected from the group consisting of hydrogen, C_{1-8} alkyl, and NR wherein R is selected from the group consisting of hydrogen, C_{1-8} alkyl, and C_{1-8} acyl:

R_9 and R_{10} are independently selected from the group consisting of hydrogen, halogen, hydroxy, acetoxy, C_{1-16} alkoxy, C_{1-16} alkyl, C_{3-8} cycloalkyl, thiol, amino, trifluoroacetamido, chloroethylnitrosoureido, and chloroethylureido:

R_{11} is selected from the group consisting of hydrogen, amino which may be unsubstituted or mono or di-substituted by C_{1-8} alkyl, C_{3-8} cycloalkyl, C_{2-8} acyl, t-butylacyl, C_{1-8} alkoxy, t-butyloxycarbonyl, trifluoroacyl, C_{7-12} aralkyl, C_{6-12} aryl, and a naturally occuring or synthetic amino acid; mono or dibenzylated amino, azido, acylated amino, trifluoroacylated amino, morpholino, cyano substituted morpholino, mono-, di-, tri- or tetra-methoxy substituted morpholino, mono-, di-, tri- or tetra-acetoxy substituted morpholino, hydroxyl, hydrogen, halogen, acetoxy, C_{1-16} alkoxyl, C_{3-8} cycloalkyl, thiol, sulfide; a group of the formula $NH(CH_2)_nCH(OR)_2$ wherein R is selected from the group consisting of C_{1-16} alkyl, C_{1-16} acyl and C_{7-16} aroyl and wherein n is 0 to 5.

chloroalkylnitrosoureido of the formula $NH(CO)N(NO)(CH_2)_nCH_2Cl$ wherein n is 0 to 4, and $NH(CH_2)_2$ $OCH_2CH(OA_c)_2$:

R^{12} is selected from the group consisting of hydrogen, hydroxyl or its tetrahydropropyl ether (-OTHP), mesylate, tosylate, halogen, mono or oligosaccharides, C_{1-8} alkoxy, amino, mono or dialkylated amino in which each alkyl contains 1 to 16 carbon atoms, trifluoroacetamido, C_{1-16} alkoxy, C_{3-8} cycloalkyl, C_{2-8} haloalkylacetate, benzoate which may be unsubstituted or substituted with nitro, one of the group consisting of p-nitrobenzoate, acetoxy, trifluoroacetoxy, chloroalkylnitro-soureido of the formula $NH(CO)N(NO)(CH_2)_nCH_2Cl$ wherein n is 0 to 4, and $NH(CH_2)_2$ $OCH_2CH(OA_c)_2$.

R5 and R8 can also be independently selected from a 5 or 6 membered aromatic or non-aromatic heterocycle containing one or more heteroatoms, selected from the group consisting of O, S, N, SO,

SO_2, P, PO and NR wherein R is selected from the group consisting of hydrogen, hydroxyl, C_{1-8} acyl, C_{1-4} alkyl and C_{6-12} aryl, said heterocycle being optionally substituted with one or more halogens, hydroxy, C_{6-18} aryl sulfone, cyano, C_{1-16} alkoxy, C_{1-16} alkyl, nitro, C_{1-16} hydroxyalkyl, amino, which may be unsubstituted or mono-or di-substituted by C_{1-8} alkyl, C_{3-8} cycloalkyl, C_{1-8} acyl, trifluoroacyl, C_{7-18} aralkyl, C_{6-18} aryl, C_{2-8} alkenyl, C_{2-8} alkynyl and hydroxy.

2. A compound according to claim 1 wherein

X_1 and X_2 are independently selected from the group consisting of

O,

S, and

NH;

X_3 is selected from the group consisting of

O,

S,

C,

SO,

SO_2,

NH,

NO, and NOH

X_4 is selected from the group consisting of

CQ,

N, and

NO,

R_1, R_2, R_3, and Q are independently selected from the group consisting of

hydrogen,

hydroxyl,

C_{1-4} alkoxyl,

tosyl,

triflate,

fluorine,

chlorine,

amino,

aminoalkylaminoalcohol of formula $NH(CH_2)_nNH(CH_2)_mOH$ wherein n and m are independently 1 to 3,

aminoalkylaminoalkylchloride of formula $NH(CH_2)_nNH(CH_2)_mCl$ wherein n and m are independently 1 to 3,

chloroalkylnitrosoureido of the formula $NH(CO)N(NO)(CH_2)_n CH_2 Cl$, a group of the formula -O-C(R)=O,wherein n is 0 to 4, and wherein and wherein R is selected from the group consisting of

hydrogen,

C_{1-6} alkyl,

and C_{6-12} aryl;

Z is one of C-R_6, orC-R_7;

R_6 is selected from the group consisting of

hydrogen,

C_{1-8} hydroxyalkyl,

C_{1-8} dihydroxyalkyl,

squaric acid,

C_{1-16} alkyl squarate,

C_{1-4} alkyl,

acyl of the formula -C(R)=O, wherein R is selected from the group consisting of

hydrogen,

C_{1-8} alkyl,

C1-8 hydroxyalkyl,

squaric acid

C_{1-4} alkyl squarate,

C_{2-8} alkoxyalkyl,

C_{2-12} acyloxyalkyl and

amino which may be unsubstituted or mono-

or di-substituted with C_{1-8}

alkyl, C_{3-8} cycloalkyl, C_{1-8} acyl,

C_{1-8} trifluroacyl, C_{7-12} aralkyl or C_{6-12} aryl;

a group of the formula -C(OR)=O, wherein R is selected from the group consisting of

hydrogen,

C_{1-8} alkyl,

C_{6-12} aryl,

C_{7-12} aralkyl; and

a group of the formula $-CH_2C(OR)=O$, wherein R is selected from the group consisting of

hydrogen,

straight or branched C_{1-8} alkyl, and

amino which may be unsubstituted

or mono- or di-substituted with

C_{1-8} alkyl, C_{3-8} cycloalkyl, C_{1-8} acyl,

trifluoroacyl, C_{7-12} aralkyl or C_{6-12} aryl;

A 5 or 6 membered aromatic or non aromatic heterocycle containing one or more heteroatoms selected from the group consisting of O, S, N, NO, and NH; said heterocycle being optionally substituted with one or more halogens, hydroxy, C_{1-8} alkoxy, C_{1-8} alkyl, C_{1-8} hydroxyalkyl, amino, which may be unsubstituted or mono- or disubstituted by C_{1-4} alkyl, C_{3-5} cycloalkyl, C_{1-8} acyl, trifluoroacyl, C_{6-12} aryl, and hydroxy;

R_7 is selected from the group consisting of

hydrogen,
fluorine,
C_{1-4} alkyl
C_{1-4} alkoxy,
cyano,
acyl of the formula -C(R)=O, wherein R is selected from the group consisting of
hydrogen,
C_{1-8} alkyl,
C_{1-8} hydroxyalkyl,
C_{2-8} acyloxyalkyl,
amino,
cyano,
a group of the formula -C(OR)=O, wherein R is selected from the group consisting of
hydrogen,
C_{1-8} alkyl,
C_{6-12} aryl,
C_{1-8} alkenyl;

R_5 and R_8 are independently selected from the group consisting of

hydrogen,
halogen,
hydroxyl,
C_{1-8} alkoxy,
C_{2-8} acetylenyl,
C_{2-8} alkenyl,
cyano,
a group of the formula -O-C(R)=O, wherein R is selected from the group consisting of
hydrogen, and
C_{1-8} alkyl;
acyl of the formula -C(R)=O, wherein R is selected from the group consisting of
hydrogen,
thiol,

C_{1-8} alkyl,

C_{1-8} hydroxyalkyl,

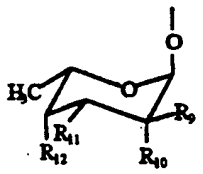
amino;

a group of the formula -C(OR)=O, wherein R is selected from the group consisting of

hydrogen, glucosamine,and

C_{1-8}alkyl,

and a saccharide of formula



wherein

R_9 and R_{10} are independently selected from the group consisting of

hydrogen,

fluorine,

chlorine,

hydroxyl,

amino, and

trifluoroacetamido;

R_{11} is selected from the group consisting of

amino which may be unsubstituted or mono-or di-substituted with C_{1-8} acetoxy, C_{1-8} alkyl, C_{3-8} cycloalkyl, C_{2-8} acyl, trifluoroacyl, C_{7-12} aralkyl or C_{6-12} aryl;

morpholino,

cyano substituted morpholino,

mono-, di-, tri-, or tetra-methoxy substituted morpholino,

hydroxyl,

mono or dialkylated amino with 1 to 16 carbons,

C_{1-8} alkoxyl,

a group of the formula $NH(CH_2)_nCH(OR)_2$ wherein R is independently selected from the group consisting of C_{1-8} alkyl, C_{1-8} acyl or C_{7-12} aroyl and wherein n is 1 to 5;

chloroalkylnitrosoureido of the formula

$NH(CO)N(NO)(CH_2)_nCH_2Cl$ wherein n is 0 to 4,

$NH(CH_2)_2$ $OCH_2(OA_c)_2$,

fluorine; and

R_{12} is selected from the group consisting of

hydroxyl or its tetrahydropyranyl ether,

halogen,

mono or oligosaccharide selected from the group consisting of from rhodosamine, cinerulose-B, L-cinerulose, D-cinerulose, cinerulose A, amicetose, aculose, rednose, rhodinose, 2-deoxyfucose, daunosamine;

and

trifluoroacetyldaunosamine,

amino,

trifluoroacetamido,

mono or dimethylated amino,

C_{1-8} alkoxy,

benzoate,

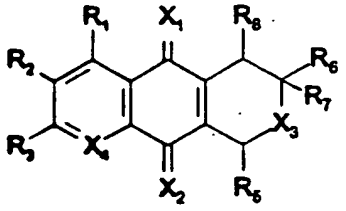
p-nitrobenzoate,

chloroalkylnitrosourea,

acetoxy and

trifluoroacetoxy.

3. A compound of the formula



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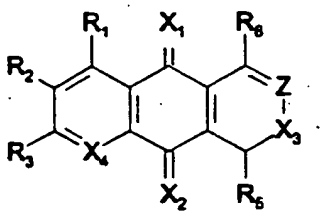

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X_1 and X_2 are independently selected from the group consisting of

0, and

NH;

X_3 is selected from the group consisting of

0,

S,

S0, and

NO;

X_4 is selected from the group consisting of CQ, N, and NO,

R_1, R_2, R_3, and Q are independently selected from the group consisting of

hydrogen,

hydroxy,

methoxy,

aminoethylaminoethanol

aminoethylaminoethylchloride

chloroalkylnitrosoureido of the formula

$NH(CO)N(NO)(CH_2)_nCH_2Cl$, wherein n is 0 to 2,

amino, and

fluorine;

Z is one of C-R_6 or C-R_7;

R_6 is selected from the group consisting of

C_{1-4} alkyl,

C_{1-4} hydroxyalkyl,

C_{1-4} dihydroxyalkyl,

acyl of the formula -C(R)=0, wherein R is selected from the group consisting of

methyl,

hydroxymethyl,

acyloxymethyl and

amino;

a group of the formula -C(OR)=O, wherein R is selected from the group consisting of

hydrogen,

methyl and

ethyl;

a group of the formula $-CH_2C(OR)=O$, wherein R is selected from the group consisting of

hydrogen,

methyl and

ethyl;

A 5 or 6 membered aromatic or non aromatic heterocycle containing one or more heteroatoms selected from the group consisting of O,S, N, NO, and NH said heterocycle being optionally substituted with one or more halogens, hydroxy, C_{1-4} alkoxy, C_{1-4} alkyl, C_{1-4} hydroxyalkyl, amino which may be unsubstituted or mono- or disubstituted by methyl, cyclopropyl, C_{2-8} acyl, and hydroxy;

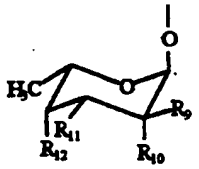
R_7 is selected from the group consisting of

hydrogen,

fluorine,

methyl,
methoxy,
cyano,
acyl of the formula -C(R)=0, wherein R is selected from the group consisting of
hydrogen,
C_{1-5} alkyl,
C_{1-8} hydroxyalkyl,
amino,
cyano,
a group of the formula -C(OR)=0, wherein R is selected from the group consisting of
hydrogen,
C_{1-5} alkyl,
C_{6-12} aryl,
C_{1-4} alkenyl;

R_5 and R_8 are independently selected from the group consisting of
hydrogen,
halogen,
hydroxy,
methoxy,
cyano,
acetate,
acetyl and
a saccharide of formula



wherein
R_9 and R_{10} are independently selected from the group consisting of
hydrogen,
fluorine, and
iodine
R_{11} is selected from the group consisting of
hydroxyl,
acetoxy,
amino,

dimethylamino,
trifluoroacetamido,
morpholino,
cyano substituted morpholino,
mono-, di-, tri-, or tetra-methoxy substituted morpholino,
a group of the formula $NH(CH_2)_nCH(OR)_2$ wherein R is selected from the group consisting of C_{1-4} alkyl C_{1-4} acyl or C_{7-8} aroyl and wherein n is 2 to 5,
chloroalkylnitrosoureido of the formula $NH(CO)N(NO)(CH_2)_nCH_2Cl$, wherein n is 0 to 4,
$NH(CO_2)OCH_2)CH_2CH(OA_c)_2$; and

R_{12} is selected from the group consisting of
hydroxyl or its tetrahydropyranyl ether,
benzoate,
acetoxy,
p-nitrobenzoate,
amino,
trifluoroacetamido,
chloroethylnitrosoureido,
fluorine, and
iodine.

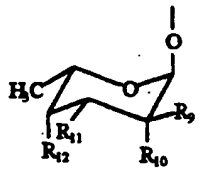
4. A compound according to claim 1, wherein
X_1 and X_2 are both oxygen;
X_3 is
O, or
S;
X_4 is selected from the group consisting of N, NO, or CQ;
R_1, R_2, R_3 and Q are each independently selected from the group consisting of hydrogen, fluorine, and hydroxyl;
Z is one of C-R_6 or C-R_7;
R_6 is selected from the group consisting of
methyl,
ethyl,
hydroxymethyl,
1,2 dihydroxyethyl,

acyl of the formula -C(R)=O, wherein R is selected from the group consisting of
methyl, fluoromethyl, difluoromethyl,
hydroxymethyl,
acetoxymethyl, and
bromomethyl;

A 5 or 6 membered aromatic or non aromatic heterocycle containing one or more heteroatoms selected from the group consisting of O, S, N, NH, said heterocycle being optionally substituted with one or more fluorine, hydroxy, methoxy, methyl, hydroxymethyl, amino and acylamino groups.

R_7 is selected from the group consisting of
hydrogen,
fluorine,
methyl, and
cyano,

R_5 and R_8 are independently selected from the group consisting of
hydrogen,
hydroxyl,
bromine,
chlorine,
cyano,
acetate,
acetyl, and
a saccharide of the formula



wherein

R_9 and R_{10} are independently selected from the group consisting of
hydrogen,
fluorine, and
iodine

R_{11} is selected from the group consisting of
amino,

hydroxy,
dimethylamino,
acetoxy,
trifluoroacetamido,
morpholino,
cyano substituted morpholino,
methoxymorpholino and
a group of the formula $NH(CH_2)_nCH(OR)_2$ wherein R is selected from a group consisting of methyl, C_{1-8} acyl or benzoyl and wherein n is 3 to 5, chloroalkylnitrosoureido of the formula $NH(CO)N(NO)(CH_2)_nCH_2Cl$, wherein n is 0 to 4, and $NH(CH_2)OCH_2CH(OA_c)_2$
R_{12} is hydroxyl or iodine.

5. A compound according to claim 1 wherein :
X_1 and X_2 are both oxygen;
X_3 is O, or S;
X_4 is CQ;
R_2 and R_3 are both hydrogen;
R_1 and Q are independently selected from the group consisting of hydrogen, fluorine, and hydroxyl;
Z is one of C-R_6 or C-R_7;
R_6 is selected from the group consisting of
ethyl,
hydroxymethyl,
1,2-dihydroxyethyl,
acyl of the formula -C(R)=O, wherein R is selected from the group consisting of
methyl, fluoromethyl, difluoromethyl,
hydroxymethyl;
R_7 is hydrogen;
R_5 and R_8 are independently selected from the group consisting of
hydrogen,
hydroxyl and
acetyl.

6. A compound according to claim 1 wherein :
X_1 and X_2 are both oxygen;
X_3 is O, or S;

X_4 is CQ,

R_2 and R_3 are both hydrogen;

R_1 and Q are independently selected from the group consisting of hydrogen, fluorine, and hydroxyl;

Z is one of C-R_6 or C-R_7;

R_6 is selected from the group consisting of

ethyl,

hydroxymethyl,

1,2-dihydroxyethyl,

carbonyl squarate, and

acyl of the formula -C(R)=0, wherein R is selected from the group consisting of

methyl,

fluoromethyl,

difluoromethyl, and

hydroxymethyl;

R_7 is selected from the group consisting of

hydrogen,

methyl,

or fluorine,

R_5 and R_8 are independently selected from the group consisting of

hydrogen,

hydroxyl,

bromine,

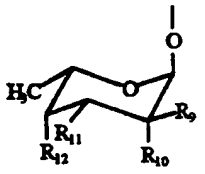
chlorine,

cyano,

acetate,

acetyl and

a saccharide of the formula



wherein

R_9 and R_{10} are independently selected from the group consisting of

hydrogen,

fluorine, and

iodine

R_{11} is selected from the group consisting of

hydroxyl,

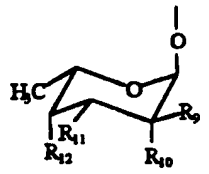
acetoxy,
amino,
dimethylamino,
trifluoroacetamido,
morpholino,
cyano substituted morpholino,
methoxymorpholino,

R_{12} is selected from the group consisting of
acetoxy,
hydroxyl,
hydrogen, and
iodine,
with the proviso that at least one of R_5 and R_8 is saccharide;

7. A compound according to Claim 5 wherein R_5 is hydrogen;

8. A compound according to Claim 5 wherein R_5 is hydroxyl;

9. A compound according to Claim 4 wherein both R_5 and R_8 are independently a saccharide of the formula:



wherein
R_9 and R_{10} are independently selected from
hydrogen,

fluorine, and
iodine;

R_{11} is selected from
amino,
dimethylamino
ammonium chloride,
trifluoroacetamido,
morpholino,
cyano substituted morpholino,
methoxy morpholino, and

R_{12} is selected from the group consisting of
hydrogen,
hydroxyl,
iodine, and
acetoxy;

10. A compound according to claim 6 wherein one of R_5 and R_8 is saccharide.

11. A compound according to claim 9 wherein R_{11} is selected from the group consisting of hydroxyl, amino, and trifluoroacetamido;

12. A compound according to claim 10 wherein R_{11} is selected from the group consisting of hydroxyl, amino, and trifluoroacetamido;

13. A compound according to claim 3 wherein X_3 is oxygen;

14. A compound according to claim 3 wherein X_3 is sulfur;

15. A compound according to Claim 13 wherein both R_5 and R_8 are independently saccharide;

16. A compound according to claim 13 wherein one of R_5 and R_8 is saccharide.

17. A compound according to Claim 14 wherein both R_5 and R_8 are independently saccharide;

18. A compound according to claim 10 wherein one of R_5 and R_8 is saccharide.

19. A compound according to claim 12 wherein R_8 is hydrogen.

20. A compound according to claim 13 wherein R_8 is hydrogen.

21. A compound according to claim 14wherein R_8 is hydrogen.

22. A compound according to claim 15 wherein R_8 is hydrogen.

23. A compound according to claim 16 wherein R_8 is hydrogen.

24. A compound according to claim 17 wherein R_8 is hydrogen.

25. A compound according to claim 18 wherein R_8 is hydrogen.

26. A compound according to claim 1, wherein X_3 is 0 or 5; and Z is one of C-R_6 or C-R_7.

27. A compound according to claim 26, wherein X_3 is O; and R_5 is methoxy or 3-(tetraethyl-3,3-bis phosphonic ester) propriamido-2-yl ethoxy.

28. A compound according to claim 3 wherein X_3 is O or S; and Z is one of C-R_6 or C-R_7.

29. A compound according to claim 28 wherein X_3 is O; and R_5 is methoxy or 3-

(tetraethyl-3,3-bis phosphonic ester) propriamido-2-yl ethoxy.

30. A compound according to claim 1 selected from the group consisting of

Methyl (5,10-dioxo-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone (BCH-1125);

Methyl (7-hydroxy-5,10-dioxo-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone (BCH-1129);

Methyl (6-hydroxy-5,10-dioxo-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;

Monofluoromethyl (5,10-dioxo-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;

Bromomethyl (5,10-dioxo-5,10-dihydronaphtho [2,3-C] pyran-3-yl) ketone;

2-[4,-Hydroxy-1',2',-dioxo-3'- cyclobutenoxy] methyl (5,10- dioxo-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;

Trans-3-aceto-1-methoxy-1,2,3,4-tetrahydro-(2-thia)anthracene-5,10-dione and cis-3-aceto-1-methoxy-1,2,3,4-tetrahydro-(2-thia)anthracene-5,10-dione;

cis-3-aceto-1-methoxy-1,2,3,4-tetrahydro-(2-thia) anthracene-5,10-dione and trans-3-aceto-1-methoxy-1,2,3,4-tetrahydro-(2-thia) anthracene-5,10-dione;

(1'S,1S,3R)-1-(2',3',6'-trideoxy-3'-amino-L-lyxohexopyranose)-3-(2-aza-3-aminothiazolyl)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho [2,3-C] pyran;

(1'S,1R,3S)-1-(2',3',6'-trideoxy-3'-amino-L-lyxohexopyranose)-3-(2-aza-3-aminothiazolyl)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho [2,3-C] pyran

Methyl (1-hydroxy-5,10-dioxo-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone (BCH-1148);

trans-3-aceto-1-hydroxy-1,2,3,4-tetrahydro-(2-thia) anthracene-5,10-dione and cis-3-aceto-1-hydroxy-1,2,3,4-tetrahydro-(2-thia) anthracene-5,10-dione;

1'S,1S,3R methyl (5,8-dioxo-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-3,4,5,10- tetrahydrobenzo [2,3-C] pyran-3-yl) ketone;

1'S,1R,3S methyl (5,8-dioxo-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-3,4,5,10-tetrahydrobenzo [2,3-C] pyran-3-yl) ketone;

(1'S,1S,3R) methyl (5,8-dimethoxy-1-(2',3',4',6'-tetradeoxy-3'4'-diacetoxy-L-Lyxohexo-pyranose)-3,4,-dihydrobenzo [2,3-C] thiopyran-3-yl);

(1'S,1R,3S) methyl (5,8-dimethoxy-1-(2',3',4',6'-tetradeoxy-3',4'-diacetoxy-L-Lyxohexopyranose)-3,4,-dihydrobenzo [2,3-C] thiopyran-3-yl);

(1'S,1S,3R) methyl (5,8-dimethoxy-1-(2',3',4',6'-tetradeoxy-3',4'-diacetoxy-L-lyxohexopyranose)-3,4,-dihydrobenzo [2,3-C] thiopyran-3-yl) ketone;

(1'S,1R,3S) methyl (5,8-dimethoxy-1-(2',3',4',6'-tetradeoxy-3',4'-diacetoxy-L-lyxohexopyranose)-3,4,5,8, tetrahydrobenzo [2,3-C] thiopyran-3-yl) ketone;

1'S, 1S, 3R- Methyl (5,10-dioxo-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'O-p-nitrobenzoyl-L-lyxohexopyranose)-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;

1'S, 1R, 3S- Methyl (5,10-dioxo-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'O-p-nitrobenzoyl-L-lyxohexopyranose)-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;

1'S, 1R, 3S Methyl (5,10-dioxo-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-7-hydroxy-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;

1'S, 1S, 3R Methyl (5,10-dioxo-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-7-hydroxy - 3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;

(1'S,1S,3R)-Bromomethyl (5,10-dioxo-1-(2',3',6'-trideoxy-4'-O-P-nitrobenzoyl-3'-trifluoroacetamido-L-lyxohexopyranose)-(3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;

(1'S,1R,3S)-Bromomethyl (5,10-dioxo-1-(2',3',6'-trideoxy-4'-O-P-nitrobenzoyl-3'-trifluoroacetamido-L-lyxohexopyranose)-(3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;

(1'S,1S,3R) -2-[4'-hydroxy-1',2'-dioxo-3'-cyclobutenoxy] methyl (5,10-dioxo-1-[2",3",6"-trideoxy-4"-O-p-nitrobenzoyl-3'-trifluoroacetamido-L-lyxohexopyranose]-3,4,5,10-tetrahydronaphtho [2,3,C] pyran-3-yl) ketone;

(1'S,1R,3S) -2-[4'-hydroxy-1',2'-dioxo-3'-cyclobutenoxy] methyl (5,10-dioxo-1-[2",3",6"-trideoxy-4"-O-p-nitrobenzoyl-3'-trifluoroacetamido-L-lyxohexopyranose]-3,4,5,10-tetrahydronaphtho [2,3,C] pyran-3-yl) ketone;

(1'S,1R,3S)-1-(2',3',6'-trideoxy-4'-O-p-nitrobenzoyl-3'-trifluoroacetamido-L-lyxohexopyranose)-3-(2-bromoacetyl)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-C]-pyran;

(1'S, 1R, 3S)-1-(2',3',6'-trideoxy-4'-O-p-nitrobenzoyl-3'-trifluoroacetamido-L-lyxohexopyranose)-3-(2-aza-3-aminothiazolyl)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-(2,3-C)-pyran;

(1'S,1R,3S)-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-p-nitrobenzoyl-L-lyxohexopyranose)-3-(2-aza-3-acetamidothiazolyl)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-C]-pyran;

(1'S,1S,3R)-1-(2',3'-6'-trideoxy-4'-p-nitrobenzoyl-3'-trifluoro-acetamido-L-lyxohexopyranose)-3-(2-bromoacetyl)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho [2,3-C] pyran;

(1'S,1S,3R)-1-(2',3'-6'-trideoxy-4'-O-p-nitrobenzoyl-3'-trifluoroacetamido-L-lyxohexopyranose)-3-(2-aza-3-acetamido)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-C]-pyran;

(1'S,1R,3S) methyl (1-[2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexo-pyranose]-5,10-dioxo-3,4,5,10-tetrahydro-7-methyl-9-aza naphtho [2,3-C] pyran-3-yl ketone;

(1'S,1S,3R) methyl (1-[2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexo-pyranose]-5,10-dioxo-3,4,5,10-tetrahydro-7-methyl-9-aza naphtho [2,3-C] pyran-3-yl ketone;

(1'S,1R,3S)-methyl-1-(2',6'-dideoxy-3',4'-di-O-p-nitrobenzoyl-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;

(1'S,1S,3R)-methyl-1-(2',6'-dideoxy-3',4'-di-O-p-nitrobenzoyl-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;

(1'S, 1R, 3R)-5,10-dioxo-3-ethyl-1-(2',3',4',6'-tetradeoxy-3',4'-diacetoxy-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho [2,3-C] pyran;

(1'S, 1S, 3S)-5,10-dioxo-3-ethyl-1-(2',3',4',6'-tetradeoxy-3',4'-diacetoxy-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho [2,3-C] pyran;

(1'S,1S,3R) methyl (5,8-dioxo-1-(2',3', 4',6'-tetradeoxy-3',4'-diacetoxy-L-lyxohexopyranose)-3,4,5,10-tetrahydronaphtho [2,3-C] thiopyran-3-yl) ketone;

(1'S,1R,3S) methyl (5,8-dioxo-1-(2',3', 4',6'-tetradeoxy-3',4'-diacetoxy-L-lyxohexopyranose)-3,4,5,10-tetrahydronaphtho [2,3-C] thiopyran-3-yl) ketone;

1'S, 1R, 3S Methyl (5,10-dioxo-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-hydroxy-L-lyxohexopyranose)-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;

1'S, 1R, 3S Methyl (5,10-dioxo-1-(2',3',6'-trideoxy-3'-amino-4'-hydroxy-L-lyxohexopyranose)-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;

1'S, 1S, 3R Methyl (5,10-dioxo-1-(2',3',6'-trideoxy-3'-Trifluoroacetamido-4'-hydroxy-L-lyxohexopyranose)- 3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;

1'S, 1S, 3R Methyl (5,10-dioxo-1-(2',3',6'-trideoxy-3'-amino-4'-hydroxy-L-lyxohexopyranose)-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;

1'S, 1R, 3S Methyl (5,10-dioxo-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-7-hydroxy - 3,4,5,10-tetrahydro [2,3-C] pyran-3-yl) ketone;

1'S, 1R, 3S Methyl (5,10-dioxo-1-(2',3',6'-trideoxy-3'- amino-L-lyxohexopyranose)-7-hydroxy-3,4,5,10-tetrahydro [2,3-C] pyran-3-yl) ketone;

(1'S,1S,3R) methyl (5,10-dioxo-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-7-hydroxy - 3,4,5,10-tetrahydro [2,3-C] pyran-3-yl) ketone;

(1'S,1S,3R) methyl (5,10-dioxo-1-(2',3',6'-trideoxy-3'- amino-L-lyxohexopyranose)-7-hydroxy- 3,4,5,10- tetrahydro [2,3-C] pyran-3-yl) ketone;

(1'S,1R,3S)-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3-(2-aza-3-acetamidothiazolyl)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho [2,3-C] pyran;

(1'S,1R,3S)-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3-(2-aza-3-acetamidothiazol)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho [2,3-C] pyran;

(1'S,1S,3R)-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3-(2-aza-3-acetamido- thiazolyl)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-C]-pyran;

(1'S,1S,3R)-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3-(2-aza-3-aminothiazolyl)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-C]-pyran;

(1'S,1R,3S) Methyl(1-(2',3',6'-trideoxy-3'-amino-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10-tetrahydro-7-methyl-9-azanaphtho-[2,3-C]-pyran-3-yl) ketone;

(1'S,1S,3R) Methyl(1-(2',3',6'-trideoxy-3'-amino-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10-tetrahydro-7-methyl-9-azanaphtho-[2,3-C]-pyran-3-yl) ketone;

(1'S,1R,3S) methyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-hydroxy-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10-tetrahydro-7-methyl-9-aza naphtho [2,3-C] pyran-3-yl) ketone;

(1'S,1S,3R) methyl(1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-hydroxy-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10-tetrahydro-7-methyl-9-aza naphtho [2,3-C] pyran-3-yl) ketone;

(1'S,1R,3R) -1-(2',6'-dideoxy-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10-tetrahydronaphtho [2,3-C] pyran;

(1'S,1S,3S) -1-(2',6'-dideoxy-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10-tetrahydronaphtho [2,3-C] pyran;

(1'S,1R,3R) -1-(2',3',6'-trideoxy-3'-amino-L-lyxohexopyranose)-5,10-dioxo-3-ethyl-3,4,5,10-tetrahydronaphtho [2,3-C] pyran;

(1'S,1S,3S) -1-(2',3',6'-trideoxy-3'-amino-L-lyxohexopyranose)-5,10-dioxo-3-ethyl-3,4,5,10-tetrahydronaphtho [2,3-C] pyran;

(1'S,1R,3R) -1-(2',3',6'-trideoxy-3'-amino-L-lyxohexopyranose)-5,10-dioxo-6 or 9-hydroxy -3-ethyl-3,4,5,10-tetrahydronaphtho [2,3-C] pyran;

(1'S,1S,3S) -1-(2',3',6'-trideoxy-3'-amino-L-lyxohexopyranose)-5,10-dioxo-6 or 9-hydroxy -3-ethyl-3,4,5,10-tetrahydronaphtho [2,3-C] pyran;

(1'S,1R,3R) -1-(2',3',6'-trideoxy-3'-amino-L-lyxohexopyranose)-5,10-dioxo-6, 9-dihydroxy -3-ethyl-3,4,5,10-tetrahydronaphtho [2,3-C] pyran;

(1'S,1S,3S) -1-(2',3',6'-trideoxy-3'-amino-L-lyxohexopyranose)-5,10-dioxo-6, 9-dihydroxy -3-ethyl-3,4,5,10-tetrahydronaphtho [2,3-C] pyran;

(1'S,1R,3R) -1-(2',3',6'-trideoxy-3'- amino-2'-iodo-L-lyxohexopyranose)-5,10-dioxo-6 or 9-hydroxy -3-ethyl-3,4,5,10-tetrahydronaphtho [2,3-C] pyran;

(1'S,1S,3S) -1-(2',3',6'-trideoxy-3'- amino-2'-iodo-L-lyxohexopyranose)-5,10-dioxo-6 or 9-hydroxy -3-ethyl-3,4,5,10-tetrahydronaphtho [2,3-C] pyran;

(1'S,1R,3R) -1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-5,10-dioxo-6 or 9-hydroxy -3-ethyl-3,4,5,10-tetrahydronaphtho [2,3-C] pyran;

(1'S,1S,3S) -1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-5,10-dioxo-6 or 9-hydroxy -3-ethyl-3,4,5,10-tetrahydronaphtho [2,3-C] pyran;

(1'S,1R,3S) Methyl(1-(2',3',6'-trideoxy-3'-amino-2'-iodo-L-lyxohexopyranose)-5,10-

dioxo-6 or 9-hydroxy-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;
(1'S,1S,3R) Methyl(1-(2',3',6'-trideoxy-3'-amino-2'-iodo-L-lyxohexopyranose)-5,10-dioxo-6 or 9-hydroxy-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;
(1'S,1R,3S) Methyl(1-(2',3',6'-trideoxy-3'-amino-L-lyxohexopyranose)-5,10-dioxo-6 or 9-hydroxy-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;
(1'S,1S,3R) Methyl(1-(2',3',6'-trideoxy-3'-amino-L-lyxohexopyranose)-5,10-dioxo-6 or 9-hydroxy-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;
(1'S,1R,3S) Methyl(1-(2',3',6'-trideoxy-3'-amino-L-lyxohexopyranose)-5,10-dioxo-6, 9-dihydroxy-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;
(1'S,1S,3R) Methyl(1-(2',3',6'-trideoxy-3'-amino-L-lyxohexopyranose)-5,10-dioxo-6, 9-dihydroxy-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;
(1'S,1R,3S) Methyl(1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-5,10-dioxo-6 or 9-hydroxy-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;
(1'S,1S,3R) Methyl(1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-5,10-dioxo-6 or 9-hydroxy-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;
(1'S,1R,3S) Methyl(1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-5,10-dioxo-6, 9-dihydroxy-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;
(1'S,1S,3R) Methyl(1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-5,10-dioxo-6, 9-dihydroxy-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;
(1'S,1R,3S) Methyl(1-(2',3',6'-trideoxy-3'-amino or trifluoroacetamido-2'-iodo-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;
(1'S,1S,3R) Methyl(1-(2',3',6'-trideoxy-3'-amino or trifluoroacetamido-2'-iodo-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;
(1'S,1R,3R) Methyl(1-(2',3',6'-trideoxy-3'-amino or trifluoroacetamido-2'-iodo-L-lyxohexopyranose)-5,10-dioxo-3-ethyl-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;
(1'S,1S,3S) Methyl(1-(2',3',6'-trideoxy-3'-amino or trifluoroacetamido-2'-iodo-L-lyxohexopyranose)-5,10-dioxo-3-ethyl-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;
(1'S,1S,3R)-1-(2',3',6'-trideoxy-3'-amino-L-lyxohexopyranose)-3-(2-aza-3-aminothiazolyl)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho [2,3-C] pyran;
(1'S,1R,3S)-1-(2',3',6'-trideoxy-3'-amino-L-lyxohexopyranose)-3-(2-aza-3-aminothiazolyl)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho [2,3-C] pyran

31. A compound according to claim 1 selected from the group consisting of

Methyl (5,10-dioxo-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone (BCH-1125);

Methyl (7-hydroxy-5,10-dioxo-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone (BCH-1129);

Methyl (6-hydroxy-5,10-dioxo-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;

Monofluoromethyl (5,10-dioxo-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;

Bromomethyl (5,10-dioxo-5,10-dihydronaphtho [2,3-C] pyran-3-yl) ketone;

2-[4,-Hydroxy-1',2',-dioxo-3'- cyclobutenoxy] methyl (5,10- dioxo-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;

Trans-3-aceto-1-methoxy-1,2,3,4-tetrahydro-(2-thia)anthracene-5,10-dione and cis-3-aceto-1-methoxy-1,2,3,4-tetrahydro-(2-thia)anthracene-5,10-dione;

cis-3-aceto-1-methoxy-1,2,3,4-tetrahydro-(2-thia) anthracene-5,10-dione and trans-3-aceto-1-methoxy-1,2,3,4-tetrahydro-(2-thia) anthracene-5,10-dione;

(1'S,1S,3R)-1-(2',3',6'-trideoxy-3'-amino-L-lyxohexopyranose)-3-(2-aza-3-aminothiazolyl)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho [2,3-C] pyran;

(1'S,1R,3S)-1-(2',3',6'-trideoxy-3'-amino-L-lyxohexopyranose)-3-(2-aza-3-aminothiazolyl)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho [2,3-C] pyran

32. A compound according to claim 1 selected from the group consisting of

Methyl (1-hydroxy-5,10-dioxo-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone (BCH-1148);

trans-3-aceto-1-hydroxy-1,2,3,4-tetrahydro-(2-thia) anthracene-5,10-dione and cis-3-aceto-1-hydroxy-1,2,3,4-tetrahydro-(2-thia) anthracene-5,10-dione;

33. A compound according to claim 1 selected from the group consisting of

1'S,1S,3R methyl (5,8-dioxo-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-3,4,5,10- tetrahydrobenzo [2,3-C] pyran-3-yl) ketone;

1'S,1R,3S methyl (5,8-dioxo-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-3,4,5,10-tetrahydrobenzo [2,3-C] pyran-3-yl) ketone;

(1'S,1S,3R) methyl (5,8-dimethoxy-1-(2',3',4',6'-tetradeoxy-3'4'-diacetoxy-L-Lyxohexo-pyranose)-3,4,-dihydrobenzo [2,3-C] thiopyran-3-yl);

(1'S,1R,3S) methyl (5,8-dimethoxy-1-(2',3',4',6'-tetradeoxy-3',4'-diacetoxy-L-Lyxohexopyranose)-3,4,-dihydrobenzo [2,3-C] thiopyran-3-yl);

(1'S,1S,3R) methyl (5,8-dimethoxy-1-(2',3',4',6'-tetradeoxy-3',4'-diacetoxy-L-lyxohexopyranose)-3,4,-dihydrobenzo [2,3-C] thiopyran-3-yl) ketone;

(1'S,1R,3S) methyl (5,8-dimethoxy-1-(2',3',4',6'-tetradeoxy-3',4'-diacetoxy-L-lyxohexopyranose)-3,4,5,8, tetrahydrobenzo [2,3-C] thiopyran-3-yl) ketone;

34. A compound according to claim 1 selected from the group consisting of

1'S, 1S, 3R- Methyl (5,10-dioxo-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'O-p-

nitrobenzoyl-L-lyxohexopyranose)-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;

1'S, 1R, 3S- Methyl (5,10-dioxo-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'O-p-nitrobenzoyl-L-lyxohexopyranose)-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;

1'S, 1R, 3S Methyl (5,10-dioxo-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-7-hydroxy-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;

1'S, 1S, 3R Methyl (5,10-dioxo-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-7-hydroxy - 3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;

(1'S,1S,3R)-Bromomethyl (5,10-dioxo-1-(2',3',6'-trideoxy-4'-O-P-nitrobenzoyl-3'-trifluoroacetamido-L-lyxohexopyranose)-(3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;

(1'S,1R,3S)-Bromomethyl (5;10-dioxo-1-(2',3',6'-trideoxy-4'-O-P-nitrobenzoyl-3'-trifluoroacetamido-L-lyxohexopyranose)-(3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;

(1'S,1S,3R) -2-[4'-hydroxy-1',2'-dioxo-3'-cyclobutenoxy] methyl (5,10-dioxo-1-[2",3",6"-trideoxy-4"-O-p-nitrobenzoyl-3'-trifluoroacetamido-L-lyxohexopyranose]-3,4,5,10-tetrahydronaphtho [2,3,C] pyran-3-yl) ketone;

(1'S,1R,3S) -2-[4'-hydroxy-1',2'-dioxo-3'-cyclobutenoxy] methyl (5,10-dioxo-1-[2",3",6"-trideoxy-4"-O-p-nitrobenzoyl-3'-trifluoroacetamido-L-lyxohexopyranose]-3,4,5,10-tetrahydronaphtho [2,3,C] pyran-3-yl) ketone;

(1'S,1R,3S)-1-(2',3',6'-trideoxy-4'-O-p-nitrobenzoyl-3'-trifluoroacetamido-L-lyxohexopyranose)-3-(2-bromoacetyl)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-C]-pyran;

(1'S, 1R, 3S)-1-(2',3',6'-trideoxy-4'-O-p-nitrobenzoyl-3'-trifluoroacetamido-L-lyxohexopyranose)-3-(2-aza-3-aminothiazolyl)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-(2,3-C)-pyran;

(1'S,1R,3S)-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-p-nitrobenzoyl-L-lyxohexopyranose)-3-(2-aza-3-acetamidothiazolyl)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-C]-pyran;

(1'S,1S,3R)-1-(2',3'-6'-trideoxy-4'-p-nitrobenzoyl-3'-trifluoro-acetamido-L-lyxohexopyranose)-3-(2-bromoacetyl)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho [2,3-C] pyran;

(1'S,1S,3R)-1-(2',3'-6'-trideoxy-4'-O-p-nitrobenzoyl-3'-trifluoroacetamido-L-lyxohexopyranose)-3-(2-aza-3-acetamido)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-C]-pyran;

(1'S,1R,3S) methyl (1-[2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-

lyxohexo-pyranose]-5,10-dioxo-3,4,5,10-tetrahydro-7-methyl-9-aza naphtho [2,3-C] pyran-3-yl ketone;

(1'S,1S,3R) methyl (1-[2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexo-pyranose]-5,10-dioxo-3,4,5,10-tetrahydro-7-methyl-9-aza naphtho [2,3-C] pyran-3-yl ketone;

(1'S,1R,3S)-methyl-1-(2',6'-dideoxy-3',4'-di-O-p-nitrobenzoyl-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;

(1'S,1S,3R)-methyl-1-(2',6'-dideoxy-3',4'-di-O-p-nitrobenzoyl-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;

(1'S, 1R, 3R)-5,10-dioxo-3-ethyl-1-(2',3',4',6'-tetradeoxy-3',4'-diacetoxy-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho [2,3-C] pyran;

(1'S, 1S, 3S)-5,10-dioxo-3-ethyl-1-(2',3',4',6'-tetradeoxy-3',4'-diacetoxy-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho [2,3-C] pyran;

(1'S,1S,3R) methyl (5,8-dioxo-1-(2',3', 4',6'-tetradeoxy-3',4'-diacetoxy-L-lyxohexopyranose)-3,4,5,10-tetrahydronaphtho [2,3-C] thiopyran-3-yl) ketone;

(1'S,1R,3S) methyl (5,8-dioxo-1-(2',3', 4',6'-tetradeoxy-3',4'-diacetoxy-L-lyxohexopyranose)-3,4,5,10-tetrahydronaphtho [2,3-C] thiopyran-3-yl) ketone;

35. A compound according to claim 1 selected from the group consisting of

1'S, 1R, 3S Methyl (5,10-dioxo-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-hydroxy-L-lyxohexopyranose)-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;

1'S, 1R, 3S Methyl (5,10-dioxo-1-(2',3',6'-trideoxy-3'-amino-4'-hydroxy-L-lyxohexopyranose)-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;

1'S, 1S, 3R Methyl (5,10-dioxo-1-(2',3',6'-trideoxy-3'-Trifluoroacetamido-4'-hydroxy-L-lyxohexopyranose)- 3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;

1'S, 1S, 3R Methyl (5,10-dioxo-1-(2',3',6'-trideoxy-3'-amino-4'-hydroxy-L-lyxohexopyranose)-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;

1'S, 1R, 3S Methyl (5,10-dioxo-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-7-hydroxy - 3,4,5,10-tetrahydro [2,3-C] pyran-3-yl) ketone;

1'S, 1R, 3S Methyl (5,10-dioxo-1-(2',3',6'-trideoxy-3'- amino-L-lyxohexopyranose)-7-hydroxy-3,4,5,10-tetrahydro [2,3-C] pyran-3-yl) ketone;

(1'S,1S,3R) methyl (5,10-dioxo-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-7-hydroxy - 3,4,5,10-tetrahydro [2,3-C] pyran-3-yl) ketone;

(1'S,1S,3R) methyl (5,10-dioxo-1-(2',3',6'-trideoxy-3'- amino-L-lyxohexopyranose)-7-hydroxy- 3,4,5,10- tetrahydro [2,3-C] pyran-3-yl) ketone;

(1'S,1R,3S)-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3-(2-aza-3-acetamidothiazolyl)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho [2,3-C] pyran;

(1'S,1R,3S)-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3-(2-aza-3-acetamidothiazol)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho [2,3-C] pyran;
(1'S,1S,3R)-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3-(2-aza-3-acetamido- thiazolyl)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-C]-pyran;
(1'S,1S,3R)-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3-(2-aza-3-aminothiazolyl)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-C]-pyran;
(1'S,1R,3S) Methyl(1-(2',3',6'-trideoxy-3'-amino-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10-tetrahydro-7-methyl-9-aznaphtho-[2,3-C]-pyran-3-yl) ketone;
(1'S,1S,3R) Methyl(1-(2',3',6'-trideoxy-3'-amino-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10-tetrahydro-7-methyl-9-aznaphtho-[2,3-C]-pyran-3-yl) ketone;
(1'S,1R,3S) methyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-hydroxy-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10-tetrahydro-7-methyl-9-aza naphtho [2,3-C] pyran-3-yl) ketone;
(1'S,1S,3R) methyl(1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-hydroxy-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10-tetrahydro-7-methyl-9-aza naphtho [2,3-C] pyran-3-yl) ketone;

36. A compound according to claim 1 selected from the group consisting of
(1'S,1R,3R) -1-(2',6'-dideoxy-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10-tetrahydronaphtho [2,3-C] pyran;
(1'S,1S,3S) -1-(2',6'-dideoxy-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10-tetrahydronaphtho [2,3-C] pyran;
(1'S,1R,3R) -1-(2',3',6'-trideoxy-3'-amino-L-lyxohexopyranose)-5,10-dioxo-3-ethyl-3,4,5,10-tetrahydronaphtho [2,3-C] pyran;
(1'S,1S,3S) -1-(2',3',6'-trideoxy-3'-amino-L-lyxohexopyranose)-5,10-dioxo-3-ethyl-3,4,5,10-tetrahydronaphtho [2,3-C] pyran;
(1'S,1R,3R) -1-(2',3',6'-trideoxy-3'-amino-L-lyxohexopyranose)-5,10-dioxo-6 or 9-hydroxy -3-ethyl-3,4,5,10-tetrahydronaphtho [2,3-C] pyran;
(1'S,1S,3S) -1-(2',3',6'-trideoxy-3'-amino-L-lyxohexopyranose)-5,10-dioxo-6 or 9-hydroxy -3-ethyl-3,4,5,10-tetrahydronaphtho [2,3-C] pyran;
(1'S,1R,3R) -1-(2',3',6'-trideoxy-3'-amino-L-lyxohexopyranose)-5,10-dioxo-6, 9-dihydroxy -3-ethyl-3,4,5,10-tetrahydronaphtho [2,3-C] pyran;
(1'S,1S,3S) -1-(2',3',6'-trideoxy-3'-amino-L-lyxohexopyranose)-5,10-dioxo-6, 9-dihydroxy -3-ethyl-3,4,5,10-tetrahydronaphtho [2,3-C] pyran;
(1'S,1R,3R) -1-(2',3',6'-trideoxy-3'- amino-2'-iodo-L-lyxohexopyranose)-5,10-dioxo-6 or 9-hydroxy -3-ethyl-3,4,5,10-tetrahydronaphtho [2,3-C] pyran;
(1'S,1S,3S) -1-(2',3',6'-trideoxy-3'- amino-2'-iodo-L-lyxohexopyranose)-5,10-dioxo-6 or 9-hydroxy -3-ethyl-3,4,5,10-tetrahydronaphtho [2,3-C] pyran;
(1'S,1R,3R) -1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-5,10-

dioxo-6 or 9-hydroxy -3-ethyl-3,4,5,10-tetrahydronaphtho [2,3-C] pyran;
(1'S,1S,3S) -1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-5,10-dioxo-6 or 9-hydroxy -3-ethyl-3,4,5,10-tetrahydronaphtho [2,3-C] pyran;
(1'S,1R,3S) Methyl(1-(2',3',6'-trideoxy-3'-amino-2'-iodo-L-lyxohexopyranose)-5,10-dioxo-6 or 9-hydroxy-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;
(1'S,1S,3R) Methyl(1-(2',3',6'-trideoxy-3'-amino-2'-iodo-L-lyxohexopyranose)-5,10-dioxo-6 or 9-hydroxy-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;
(1'S,1R,3S) Methyl(1-(2',3',6'-trideoxy-3'-amino-L-lyxohexopyranose)-5,10-dioxo-6 or 9-hydroxy-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;
(1'S,1S,3R) Methyl(1-(2',3',6'-trideoxy-3'-amino-L-lyxohexopyranose)-5,10-dioxo-6 or 9-hydroxy-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;
(1'S,1R,3S) Methyl(1-(2',3',6'-trideoxy-3'-amino-L-lyxohexopyranose)-5,10-dioxo-6, 9-dihydroxy-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;
(1'S,1S,3R) Methyl(1-(2',3',6'-trideoxy-3'-amino-L-lyxohexopyranose)-5,10-dioxo-6, 9-dihydroxy-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;
(1'S,1R,3S) Methyl(1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-5,10-dioxo-6 or 9-hydroxy-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;
(1'S,1S,3R) Methyl(1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-5,10-dioxo-6 or 9-hydroxy-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;
(1'S,1R,3S) Methyl(1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-5,10-dioxo-6, 9-dihydroxy-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;
(1'S,1S,3R) Methyl(1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-5,10-dioxo-6, 9-dihydroxy-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;
(1'S,1R,3S) Methyl(1-(2',3',6'-trideoxy-3'-amino or trifluoroacetamido-2'-iodo-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;
(1'S,1S,3R) Methyl(1-(2',3',6'-trideoxy-3'-amino or trifluoroacetamido-2'-iodo-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;
(1'S,1R,3R) Methyl(1-(2',3',6'-trideoxy-3'-amino or trifluoroacetamido-2'-iodo-L-lyxohexopyranose)-5,10-dioxo-3-ethyl-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;
(1'S,1S,3S) Methyl(1-(2',3',6'-trideoxy-3'-amino or trifluoroacetamido-2'-iodo-L-lyxohexopyranose)-5,10-dioxo-3-ethyl-3,4,5,10-tetrahydronaphtho [2,3-C] pyran-3-yl) ketone;
(1'S,1S,3R)-1-(2',3',6'-trideoxy-3'-amino-L-lyxohexopyranose)-3-(2-aza-3-aminothiazolyl)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho [2,3-C] pyran;
(1'S,1R,3S)-1-(2',3',6'-trideoxy-3'-amino-L-lyxohexopyranose)-3-(2-aza-3-aminothiazolyl)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho [2,3-C] pyran;

37. A compound according to Claim 1 selected from the group consisting of:

1184 (1'S, 1S, 3R)-methyl-(1-[2',3',6'-trideoxy-3'-trifluoro-acetamido-4'-hydroxy-L-lyxohexo-pyranose]-3,4,5,10-tetrahydro-naphtho[2,3-C]pyran-3-yl)ketone

1620 (1'S,1-R,3-S)-methyl-(1-[2',3',6'-trideoxy-3'-trifluoroacetamido-4'-iodo-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-C]pyran-3-yl)ketone

1648 (1'-S,1-S,3-R)-methyl-(1-[2',3',6'-trideoxy-3'-trifluoroacetamido-4'-hydroxy-L-arabino-hexopyranose)-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-C]pyran-3-yl)ketone

1649 (1'-S,1-R,3-S)-methyl-(1-[2',3',6'-trideoxy-3'-trifluoroacetamido-4'-hydroxy-L-arabino-hexopyranose)-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-C]pyran-3-yl)ketone

1666 (1'S,1R,3S)-methyl-(1-[2',6'-dideoxy-3',4'-diacetyl-2'-iodo-L-lyxohexopyranose]-3,4,5,10-tetrahydronaphtho[2,3-C]pyran-3-yl) ketone

1667 (1'S, 1S, 3R)-methyl-(1[2',6'-dideoxy-3',4'-diacetyl-2'-iodo-L-lyxohexopyranoee]-3,4,5,10-tetrahydronaphtho[2,3-C]pyran-3-yl) ketone

1673 (1'-S,1-S,3-R) and (1'-S,1-R,3-S)-methyl-(1-[2',3',4',6'-tetradeoxy-4'-trifluoroacetamido-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-C]pyran-3-yl)ketone

1998 (1S,3S,2'S,5'S)-methyl-(1-O-[N-Boc-serine-leucine-me ester]-5,10-dioxo-3,4,5,10-tetrahydronaphthaleno-[2,3-C]pyran-3-yl)ketone

2000 (1S,3S,2'S,5'S)-methyl-(1-O-[serine-leucine-me ester]-5,10-dioxo-3,4,5,10-tetrahydronaphthaleno-[2,3-C]pyran-3-yl)ketone hydrochloride

2019 (1R,3S,1'S0-methyl-(1-[2',3',4',6'-tetradeoxy-3'-trifluoroacetamido-4'-bromo-L-lyxohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphthaleno-[2,3-C]pyran-3-yl)ketone

2022 (1'S,1S,3R)-methyl-(1-[2',3',6'-trideoxy-4'-hydroxy-2'-iodo-3'-trifluoroacetamido-L-lyxohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphtho[2,3,-C]pyran-3-yl)ketone

2041 phenyl-(trans-1-methoxy-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-C]-pyran)-3-carboxamide

2046 (1R,3S,1'S)-methyl-(1-[2',3',4',6'-tetradeoxy-3'-trifluoroacetamido-4'-bromo-L-lyxohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphthaleno-[2,3-C]pyran-3-yl)ketone

2047 (1S,3R,1'S)-methyl-(1-[2',3',4',6'-tetradeoxy-3'-trifluoroacetamido-4'-bromo-L-lyxohexopyranose]-5,10-dioxo-3,4,5,10-tetranaphthaleno-[2,3-C]pyran-3-yl)ketone

2051 3-dimethylaminopropyla(1-methoxy-5,10-dihydro-1H-naphtho-[2,3-C]-pyran)-3-carboxamide

2061 (1S,2'S,3R) and (1R,2'S,3S)-methyl-(1-O-[3-pipecolinemethanol]-5,10-dioxo-3,4,5,10-tetrahydronaphthaleno-[2,3-C]pyran-3-yl) ketone hydrochloride racemic mixture

2069 methyl-(1-O-[4-pipecolinemethanol]-5,10-dioxo-3,4,5,10-tetrahydronaphthaleno-[2,3-C]pyran-3-yl)ketone hydrochloride racemic mixture

2070 (1'-S,1-R,3-S)-methyl-(1-[2',3',4',6' tetradeoxy-3'-methoxy-4'-O-methanesulfonyl-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-C] pyran-3-yl)ketone

2071 (1'-S,1-S,3-4)-methyl-(1-[2',3',4',6'-tetradeoxy-3',4'-dimethoxy-L-lyxohexopyranose)-5,10-DIOXO-3,4,5,10-tetrahydronaphtho-[2,3-C]pyran-3-yl) ketone (Tentative assignment)

2072 (1'-S,1-R,3-R)-methyl-1-[2',3',4',6'-tetradeoxy-3'-methoxy-4'O-methanesulfonyl-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10-tetrahydronaphtho-2,3-C]-pyran-3-yl-ketone

2079 (1S,1'S,3RO-methyl-(1-[2',3',4',6'-tetradeoxy-4'-trifluoroacetamido-L-lyxohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphthaleno-[2,3-C]pyran-3-yl)ketone

2087 (1R,3S,1'S) and (1S,3R,1'S)-METHYL-(1-[2',3',4',6',-tetradeoxy-3',4'-bistrifluoroacetamido-lyxo-hexopyranose]-5,10-dioxo-3,4,5,10-tetrahydro-naphthaleno-[2,3-C]pyran-3-yl)ketone

2095 (1'-S,1-S,3-R) and (1'S,1-R,3-S)-methyl-(1-[2',3',4',6'-tetradeoxy-3'-trifluoroacetamido-4'-O-methanesulfonyl-L-lyxopyranose)-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-C]pyran-3-yl)ketone

2102 (1S,3R,1'S)-methyl-(1-[2',3',4',6-tetradeoxy-3',4'-bistrifluoroacetamido-lyxo-hexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphthaleno-[2,3-C]pyran-3-yl)ketone

2104 (1R,3S,1'S)-methyl-(1-[2',3',4',6-tetradeoxy-3',4'-bistrifluoroacetamido-lyxo-hexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphthaleno-[2,3-C]pyran-3-yl) ketone

2105 (1'-S,1-S,3-R)-methyl-(1-[2',3',4''6'-tetradeoxy-3'-trifluoroacetamido-4'-O-(2-bromo-acetyl)-L-lyxopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-C] pyran-3-yl) ketone

2112 (1'S,1R,3S)-isopropyl-[1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-NAPHTO[2,3-C]-pyranyl]ketone

2113 A 4:1 Misture of (1'S,1R,3S)-methyl-(1-[2',3',6'-trideoxy-3'-trifluoroacetamido-4-iodo-L-arabino-hexopyranose)-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-C]pyran-3-yl)ketone and (1'S,1S,3R)-methyl-(1-[2',3',6'-trideoxy-3'-trifluoroacetamido-4'-iodo-beta-L-arabino-hexopyranose)-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-C]pyran-3-yl) ketone

2117 (1'S,1S,3R) and (1'S,1R,3S)-methyl-(1-[2',6'-dideoxy-3',4'-dihydroxy-L-lyxohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphtho[2,3-C]-pyran-3-yl) ketone

2118 (1'S,1S,3R) and (1'S,1R,3S)-methyl-(1-[2',6'-dideoxy-3',4'-diacetoxy-L-lyxohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphtho[2,3-C]pyran-3-yl) ketone

2121 (1'S,1S,3R)-5,10-dioxo-3-isopropoxycarbonyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho[2,3-C]-pyran

38. A compound according to Claim 1 selected from the group consisting of:

1184 (1'S, 1S, 3R)-methyl-(1-[2',3',6'-trideoxy-3'-trifluoroacetamido-4'-hydroxy-L-lyxohexopyranose]-3,4,5,10-tetrahydronaphtho[2,3-C]pyran-3-yl) ketone

1620 (1'S,1-R,3-S)-methyl-(1-[2',3',6'-trideoxy-3'-trifluoroacetamido-4'-iodo-L-

lyxohexopyranose)-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-C]pyran-3-yl) ketone

1648 (1'-S,1-S,3-R)-methyl-(1-[2',3',6'-trideoxy-3'-trifluoroacetamido-4'-hydroxy-L-arabino-hexopyranose)-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-C]pyran-3-yl) ketone

1169 (1'S, 1R, 3S) AND (1'S, 1S, 3R)-methyl-(1-[2',3',6'-trideoxy-3'-trifluoroacetamido-4'-hydroxy-L-lyxohexopyranose]-7-hydroxy-3,4,5,10-tetrahydronaphtho[2,3-C]pyran-3-yl) ketone

1666 (1'S,1R,3S)-methyl-(1-[2',6'-dideoxy-3',4'-diacetyl-2'-iodo-L-lyxohexopyranose]-3,4,5,10-tetrahydronaphtho[2,3-C]pyran-3-yl) ketone

1667 (1'S, 1S, 3R)-methyl-(1[2',6'-dideoxy-3',4'-diacetyl-2'-iodo-L-lyxohexopyranose]-3,4,5,10-tetrahydronaphtho[2,3-C]pyran-3-yl) ketone

1673 (1'-S,1-S,3-R) and (1'-S,1-R,3-S)-methyl-(1-[2',3',4',6'-tetradeoxy-4'-trifluoroacetamido-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-C]pyran-3-yl) ketone

2019 (1R,3S,1'S0-methyl-(1-[2',3',4',6'-tetradeoxy-3'-trifluoroacetamido-4'-bromo-L-lyxohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydro-naphthaleno-[2,3-C]pyran-3-yl) ketone

2046 (1R,3S,1'S)-methyl-(1-[2',3',4',6'-tetradeoxy-3'-trifluoroacetamido-4'-bromo-L-lyxohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphthaleno-[2,3-C]pyran-3-yl) ketone

2047 (1S,3R,1'S)-methyl-(1-[2',3',4',6'-tetradeoxy-3'-trifluoroacetamido-4'-bromo-L-lyxohexopyranose]-5,10-dioxo-3,4,5,10-tetranaphthaleno-[2,3-C]pyran-3-yl) ketone

2051 3-dimethylaminopropyla(1-methoxy-5,10-dihydro-1H-naphtho-[2,3-C]-pyran)-3-carboxamide

2061 (1S,2'S,3R) and (1R,2'S,3S)-methyl-(1-O-[3-pipecolinemethanol]-5,10-dioxo-3,4,5,10-tetrahydronaphthaleno-[2,3-C]pyran-3-yl) ketone hydrochloride racemic mixture

2070 (1'-S,1-R,3-S)-methyl-(1-[2',3',4',6' tetradeoxy-3'-methoxy-4'-O-

methanesulfonyl-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-C] pyran-3-yl) ketone

2071 (1'-S,1-S,3-4)-methyl-(1-[2',3',4',6'-tetradeoxy-3',4'-dimethoxy-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-C]pyran-3-yl) ketone (TENTATIVE ASSIGNMENT)

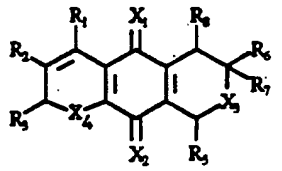
2079 (1S,1'S,3RO-methyl-(1-[2',3',4',6'-tetradeoxy-4'-trifluoroacetamido-L-lyxohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphthaleno-[2,3-C]pyran-3-yl) ketone

2087 (1R,3S,1'S) and (1S,3R,1'S)-methyl-(1-[2',3',4',6',-tetradeoxy-3',4'-bistrifluoroacetamido-lyxo-hexopyranose]-5,10-dioxo-3,4,5,10-tetrahydro-naphthaleno-[2,3-C]pyran-3-yl) ketone

2105 (1'-S,1-S,3-R)-methyl-(1-[2',3',4''6'-tetradeoxy-3'-trifluoroacetamido-4'-O-(2-bromo-acetyl)-L-lyxopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-C] pyran-3-yl) ketone

2117 (1'S,1S,3R) and (1'S,1R,3S)-methyl-(1-[2',6'-dideoxy-3',4'-dihydroxy-L-lyxohexo-pyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphtho[2,3-C]-pyran-3-yl)ketone

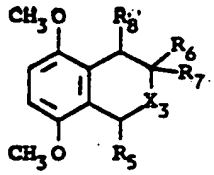
39. A process for the preparation of a compound of formula ,



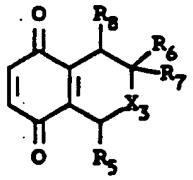
and pharmaceutically acceptable acid addition salts thereof wherein X_3 is selected from the group consisting NR, 0, or S, R_6 is methyl ketone or is as defined in claim 1; and R_1, R_2, R_3, R_5, R_6, R_7, R_8, X_1, X_2 and X_4 are as defined in claim 1

selected from the group of processes consisting of

I. 1) selecting a precurser isochroman compound of formula

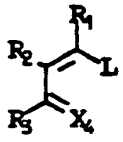


wherein R_5, R_6, R_7 and R_8 are defined as above, oxidatively demethylating said compound with an oxidant to give a quinone compound of formula



15

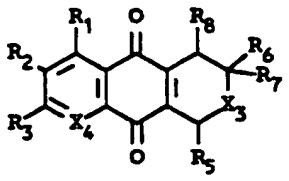
2) and cyclo-adding said quinone with a diene of formula



16

wherein L is a leaving group selected from the group consisting of halogen, tosyl, benzoyl, p-nitrobenzoyl and -OR or -SR, wherein R is selected from the group consisting of hydrogen, C_{1-16} alkyl, C_{1-16} acyl, C_{1-16} aryl, C_{1-16} alkylsilane and dimethylamino,

wherein R_1, R_2, R_3 and X_4 are as defined as above; to yield a tricyclic heteronaphthoquinone of formula

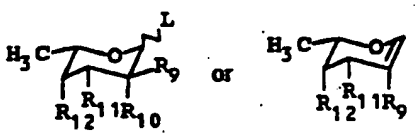


17

and

3) optionally coupling said tricyclic heteronaphthoquinone at R_5, wherein R_5 is -OH, to

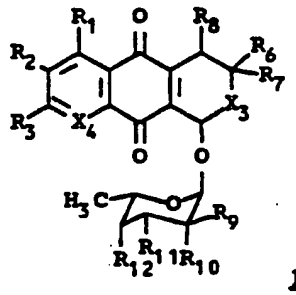
a saccharide of formula



18a 18b

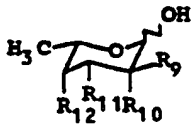
wherein R_9, R_{10}, R_{11} and R_{12} are defined as in claim 1 and L is as defined above;

to yield a tricyclic saccharide of formula



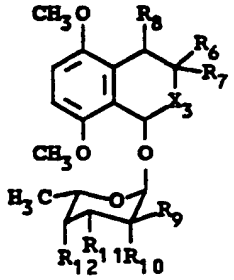
12

II. a) coupling the isochroman (14) of reaction I,1, above, wherein R_5 is H, with a saccharide of formula



20

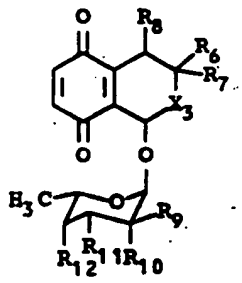
wherein R_9, R_{10}, R_{11} and R_{12} are defined as in claim 1 to yield a bicyclic saccharide of formula



21

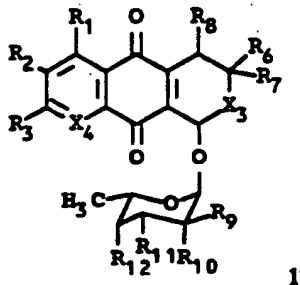
b) oxidatively demethylating the methoxy groups from formula (21) to yield a bicyclic

quinone saccharide of formula



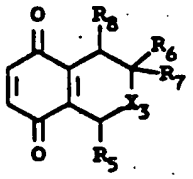
19

c) and cyclo-adding said chemical (19) with said diene (16) of reaction (I)(2) to yield the tricyclic saccharide



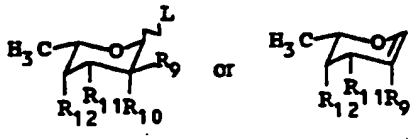
12

III. 1) coupling the quinone of formula 15,



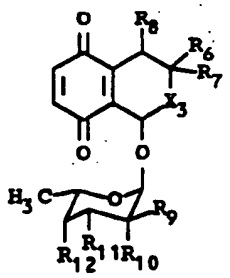
15

of step (I) (1), wherein R_5 is -OH, with a saccharide of the formula



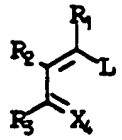
18a 18b

of step (I) (2) to yield a bicyclic quinone sacharide of the formula



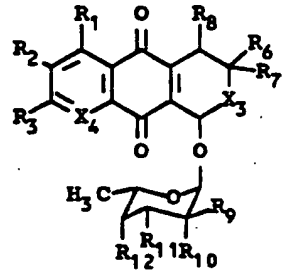
19

2) and cycloadding said quinone saccharide with the said diene of formula



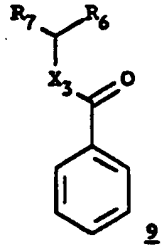
16

to yield a tricyclic saccharide of formula



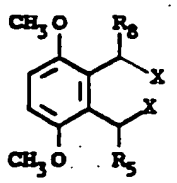
12

IV. a) selecting a precurser benzoate compound of formula



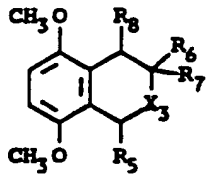
9

and condensing it with a dihalomethyl dimethoxybenzene wherein said halogens are indepently selected from the group consisting of Cl, Br and I, and X_3 is selected from the group consisting of O,S, and N;



6

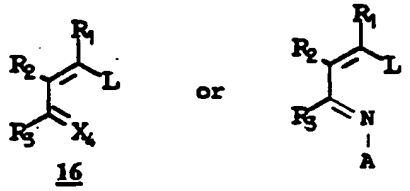
to yield a dimethoxyisochroman of formula,



14

b) oxidatively demethylating the methoxy groups from formula 14 to a bicyclic dioxoisochroman;

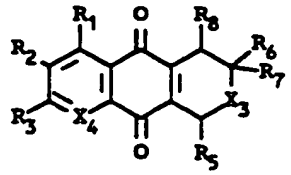
the resulting dioxoisochroman is cyclically coupled with the diene of formula



16

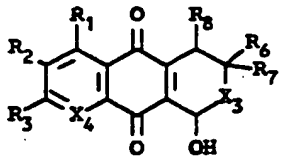
A is NR wherein R is selected from the group consiting of H, C_{1-16} alkyl, C_{7-16} aryl and L is a leaving group as defined in L.2)

to yield an anthracenedione of formula



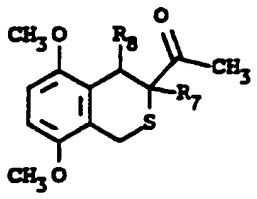
17

the resultant compound may optionally be converted to the hydroxyl form of formula



and may be optionally coupled with a saccharide of formula 20 to yield the tricyclic saccharide of formula 12;

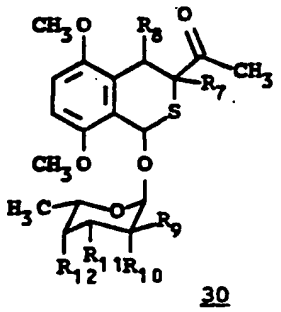
V. a dimethoxyisothiochroman of formula



may be optionally coupled with a saccharide of formula

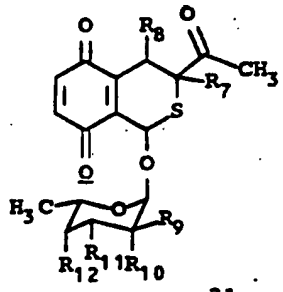
20

1) to yield a dimethoxybicyclic saccharide of formula



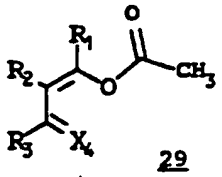
30

2) oxidatively demethylating the methoxy groups to yield a dioxobicyclic isochroman of formula



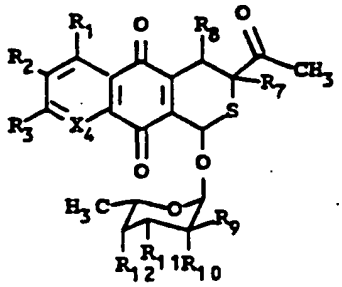
31

3) cycloadding said dioxobicyclic isothiochroman with a diene of formula 29



29

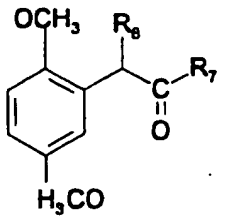
to yield a thiotricyclic saccharide of formula.



34

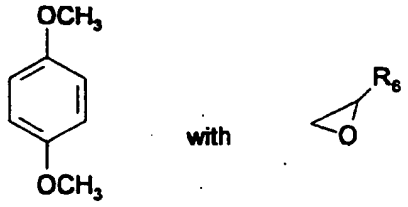
48. Process according to claim 39 comprising the further preliminary steps of a:

a) reacting

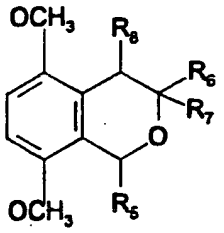


with R_8 mgX

or b)

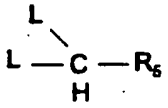


c) to yield product:

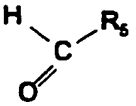


d) and further reacting said product:

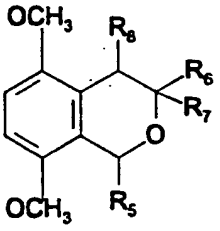
with



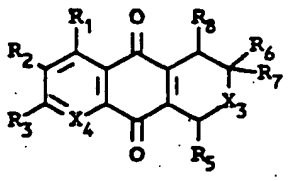
or



to yield:



41. A process, according to claim 39, for the preparation of a compound of formula,

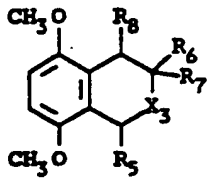


17

and pharmaceutically acceptable acid addition salts thereof,

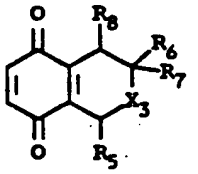
wherein X_3 is selected from the group consisting of N, S, or 0, R_6 is methyl ketone or is as defined in claim 4 and R_1, R_2, R_3, R_5, R_6, R_7, R_8, and X_4 are as defined in claim 4 which comprises the steps of

I. 1) selecting a precurser isochroman compound of formula,



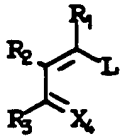
14

wherein R_5, R_6, R_7 and R_8 are defined as above; oxidatively demethylating said isochroman with an oxidant to give a quinone compound of formula,



15

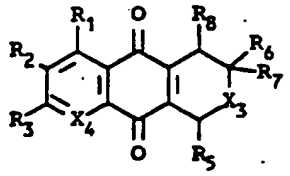
2) and cyclo-adding said quinone with a diene of formula,



16

wherein L is a leaving group selected from the group consisting of halogen, tosyl, benzoyl, p-nitrobenzoyl and -OR or -SR, wherein R is selected from the group consisting of hydrogen C_{1-16} alkyl, C_{1-16} acyl, and C_{1-16} aryl, C_{1-16} alkyl silane and dimethylamino;

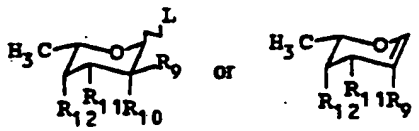
wherein R_1, R_2, R_3 and X_4 are as defined as above; to yield a tricyclic heteronaphthoquinone of formula,



17

and

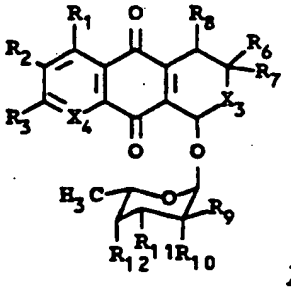
3) optionally coupling said tricyclic heteronaphthoquinone at R_5, wherein R_5 is OH, to a saccharide of formula,



18a or 18b

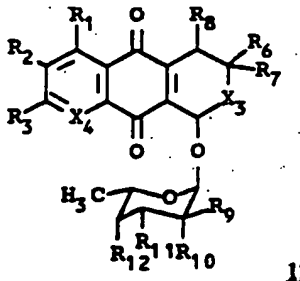
wherein R_9, R_{10}, R_{11} and R_{12} are defined as in claim 4 and L is a leaving group selected from the group consisting of halogen, benzoyl, tosyl, p-nitrobenzoyl and -OR or -SR, wherein R is selected from the group consisting of C_{1-16} alkyl, C_{1-16} acyl, C_{1-16} aryl, and C_{1-16} trialkylsilane,

to yield a tricyclic saccharide of formula,



12

42. A process according to claim 39 for the preparation of a compound of formula,

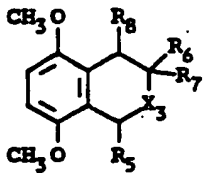


12

and pharmaceutically acceptable acid addition salts thereof,

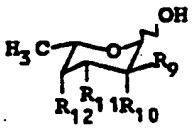
wherein X_3 is selected from the group consisting of S, or 0, R_6 is methyl ketone or is as defined in claim 4, R_5 is saccharide as defined in claim 4, and X_4, R_1, R_2, R_3, R_7, R_8, R_9, R_{10}, R_{11} and R_{12} are defined as in claim 4, which comprises the steps of

1) coupling an isochroman



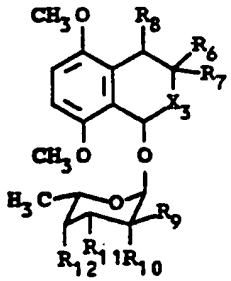
14

wherein R_5 is H and R_6, R_7 and R_8 are defined as above with a saccharide of formula,



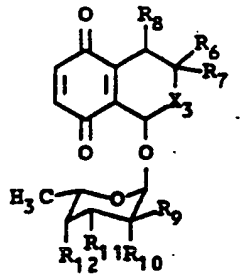
20

wherein R_9, R_{10}, R_{11} and R_{12} are defined as above to yield a bicyclic saccharide of formula,



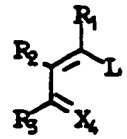
21

2) oxidatively demethylating the methoxy groups of formula (21) to yield a bicyclic quinone saccharide of formula,



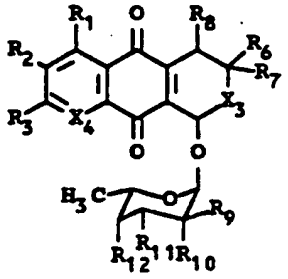
19

3) cyclo-adding said bicyclic quinone saccharide a diene of formula,



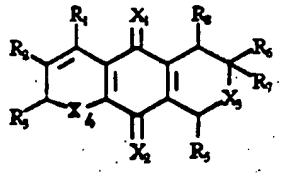
16

wherein L is a living group selected from the group consisting of halogen, tosyl, benzoyl, p-nitrobenzoyl and -OR or -SR, wherein R is selected from the group consisting of hydrogen C_{1-16} alkyl, C_{1-16} acyl, C_{1-16} aryl, C_{1-16} alkylsilane and dimethylamino, to yield a compound of formula



12

43. A process, according to claim 39, for the preparation of a compound of formula,

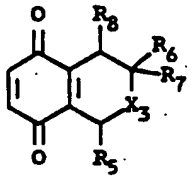


12

and pharmaceutically acceptable acid addition salts thereof,

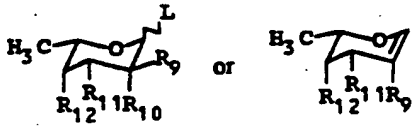
wherein X_3 is selected from the group consisting of NR, S, or 0, R_6 is methyl ketone or is as defined in claim 4, R_5 is saccharide as defined in claim 4, and R_1, R_2, R_3, R_7, R_8, R_9, R_{10}, R_{11}, R_{12}, and X_4 are defined as in claim 4; which comprises the steps of

1) coupling the quinone of formula,



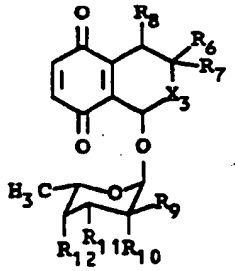
15

wherein R_5 is OH with a saccharide of formula,



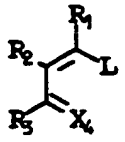
18a 18b

wherein L is a leaving group selected from the group consisting of halogen, tosyl, benzoyl, p-nitrobenzoyl and -OR or -SR, wherein R is selected from the group consisting of hydrogen C_{1-16} alkyl, C_{1-16} acyl, C_{1-16} aryl, C_{1-16} alkylsilane and dimethylamino, to yield a bicyclic quinone saccharide of the formula,



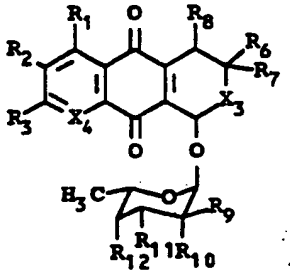
19

2) and cyclically coupling said quinone saccharide with the diene of formula, wherein L is defined as above



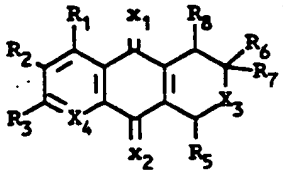
16

to yield a tricyclic saccharide of formula,



12

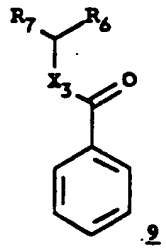
44. A process according to claim 39, for the preparation of a compound of formula,



and pharmaceutically acceptable acid addition salts thereof,

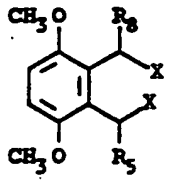
wherein X_3 is selected from the group consisting of N, O, or S, X_1 and X_2 are 0, R_5 is hydroxyl and R_1, R_2, R_3, R_6, R_7, R_8, and X_4 are defined as in claim 4, which comprises the steps of

1) selecting a precurser benzoate compound of formula,



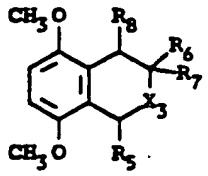
9

and condensing it with a dihalomethyl dimethoxybenzene,



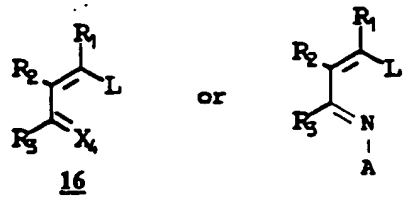
6

wherein said halogens are independently selected from the group consisting of Cl, Br and I and X_3 is selected from the group consisting of O, S, and N to yield a dimethoxyisochroman of formula,



14

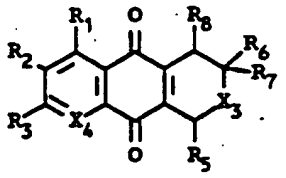
2) oxidatively demethylating the methoxy groups to yield a bicyclic dioxoisothiochroman; the resulting dioxoisothiochroman is cyclically coupled with the diene of formula,



16

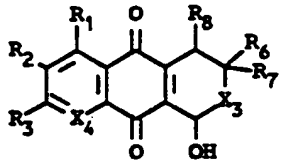
wherein A is NR and R is selected from the group consisting of H, C_{1-16} alkyl, and C_{7-16} aryl, and L is a living group selected from the group consisting of halogen, tosyl,

benzoyl, p-nitrobenzoyl and -OR or -SR, wherein R is selected from the group consisting of hydrogen C_{1-16} alkyl, C_{1-16} acyl, C_{1-16} aryl, C_{1-16} alkylsilane and dimethylamino, to yield an anthracenedione of the formula,

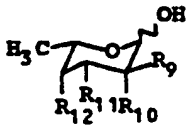


17

the resultant compound may optionally be converted to the hydroxyl-form yielding a compound of formula,

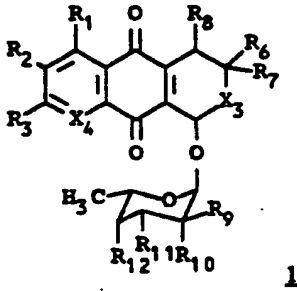


the resultant compound may be optionally coupled with a saccharide of formula,



20

wherein R_9, R_{10}, R_{11} and R_{12} are defined as in claim 4, to yield a tricyclic saccharide of formula,



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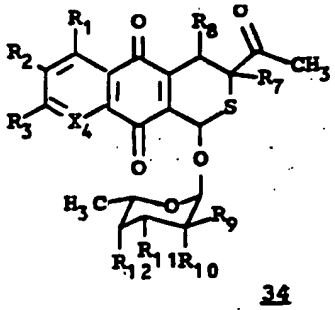
45. A process according to claim 39, for the preparation of a compound of formula,



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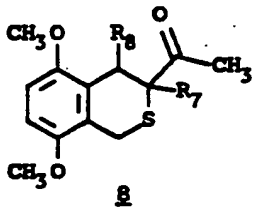
and pharmaceutically acceptable acid addition salts thereof,

wherein R_1, R_2, R_3, R_7, R_8, R_9, R_{10}, R_{11}, R_{12}, and X_4 are defined as in claim 4; which comprises the steps of

1) selecting a dimethoxythioisochroman of formula,



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and coupling it with a saccharide of formula,

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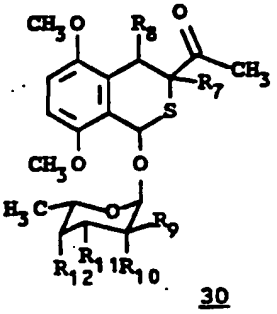
2) to yield a dimethoxybicyclic saccharide of formula,



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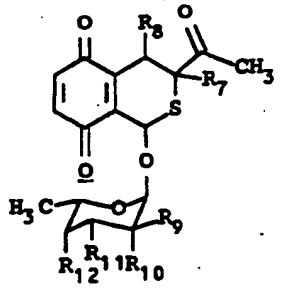
3) oxidatively demethylating the methoxy groups to yield a dioxobicyclic thioisochroman or formula,



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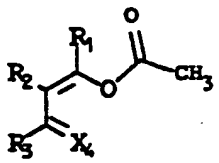
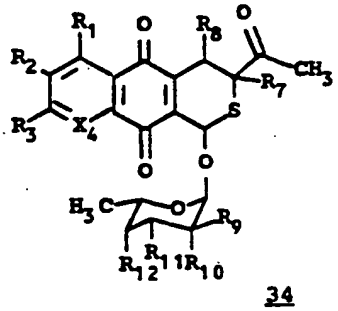
4) cycloadding said dioxobicyclic isochroman with a diene of formula,



to yield a thiotricyclic saccharide of formula,



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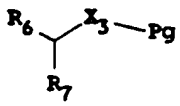
46. A process according to claim 39 which comprises a further preliminary step of

1) selecting a precurser compound of formula



wherein R_6, and R_7 are electron withdrawing groups as defined in claim 4, X_3 is O or S, and Pg is a protecting group selected from the group consisting of

acyl,

trifluoracyl,

benzoyl,

P-nitrobenzyl,

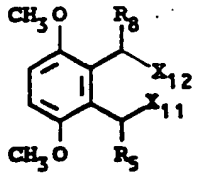
C_{1-16} alkylsilane,

C_{1-16} alyl,

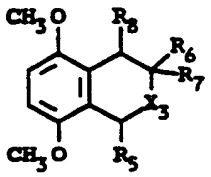
C_{1-16} acyl,

C_{1-16} aryl,

and condensing said precursor compound with a dihalomethyl dimethoxybenzene of formula



wherein X_{11} and X_{12} are independently selected from the group consisting of Cl, Br, and I, to yield a dimethoxy bicyclic precursor chemical of formula



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47. A process according to claim 39 which comprises a further step of attaching a protecting group to at least one of the moieties at positions R_1, R_2, R_3, R_6, R_7 and R_8 and positions R_9, R_{10}, R_{11}, and R_{12} of the saccharide prior to glycosylation and then removing said protecting group or groups.

48. A process according to claim 47 wherein said protected positions are at R_1, R_2 and R_3;

49. A process according to claim 39 wherein X_3 is O or S;

50. A process according to claim 41 wherein X_3 is O or S;

51. A process according to claim 42 wherein X_3 is O or S;

52. A process according to claim 43 wherein X_3 is O or S;

53. A process according to claim 44 wherein X_3 is O or S;

54. A process according to claim 39 wherein X_3 is O;

55. A process according to claim 41 wherein X_3 is O;

56. A process according to claim 42 wherein X_3 is O;

57. A process according to claim 43 wherein X_3 is O;

58. A process according to claim 44 wherein X_3 is O;

59. A process according to claim 45 wherein X_3 is O;

60. A pharmaceutical composition possessing anti-tumor activity, comprising an effective amount of at least one compound according to claim 1 and a pharmaceutical acceptable carrier.

61. A pharmaceutical composition possessing anti-tumor activity, comprising an effective amount of at least one compound according to claim 3 and a pharmaceutical acceptable carrier.

62. A pharmaceutical composition possessing anti-tumor activity, comprising an effective amount of at least one compound according to claim 4 and a pharmaceutical acceptable carrier.

63. A pharmaceutical composition possessing anti-tumor activity, comprising an effective amount of at least one compound according to claim 5 and a pharmaceutical acceptable carrier.

64. A pharmaceutical composition possessing anti-tumor activity, comprising an effective amount of at least one compound according to claim 6 and a pharmaceutical acceptable carrier.

65. A pharmaceutical composition possessing anti-tumor activity, comprising an effective amount of at least one compound according to claim 7 and a pharmaceutical acceptable carrier.

66. A pharmaceutical composition possessing anti-tumor activity, comprising an effective amount of at least one compound according to claim 8 and a pharmaceutical acceptable carrier.

67. A pharmaceutical composition possessing anti-tumor activity, comprising an effective amount of at least one compound according to claim 13 and a pharmaceutical acceptable carrier.

68. A pharmaceutical composition possessing anti-tumor activity, comprising an effective amount of at least one compound according to claim 14 and a pharmaceutical acceptable carrier.

69. A pharmaceutical composition according to claim 1, wherein said compound is

combined with an agent facilitating targetting of said combination to tumor or cancer cells.

70. A pharmaceutical composition according to claim 3, wherein said compound is combined with an agent facilitating targetting of said combination to tumor or cancer cells.

71. A compound according to claim 1 selected from the group consisting of:

(1'-S, 1'S, 3-R)-methyl-(1-[2',3',4',6' tetradeoxy-3'-methoxy-4'-O-methanesulfonyl-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10 tetrahydronaphtho-[2,3-c] pyran-3-yl) ketone BCH-2072

1-Methoxy-5,10-dioxo-5,10-dihydro-1H-naphtho[2,3-c]pyran-3-[N-(3-dimethylamino-propyl)carboxamide] (BCH-2167)

1-Methoxy-5,10-dioxo-5,10-dihydro-1H-naphtho[2,3-c]pyran-3-[N-(3-dimethylamino-propyl)carboxamide] hydrochloride monohydrate (BCH-2051)

(1S,2'S,3S,5'S)-Methyl-(1-O-[N-BOC-Serine-Leucine-Me ester]-5,10-dioxo-3,4,5,10-tetrahydro-1-H-naphtho [2,3-c] pyran-3-yl) ketone (BCH-1998)

(1S,2'S,3S,5'S)-Methyl-(1-O-[Serine-Leucine-Me ester]-5,10-dioxo-3,4,5,10-tetrahydro-1-H-naphtho [2,3-c] pyran-3-yl) ketone hydrochloride (BCH-2000)

(1S, 2'S, 3R) and (1R, 2'S, 3S)-methyl-(1-[O-serine methyl ester]-5,10-dioxo-3,4,5,10-tetrahydronaphtaleno [2,3-C] pyran-3-yl) ketone hydrochloride. (BCH-1654)

(1S, 2'S, 3R) and (1R, 2'S, 3S)-methyl-(1-[O-N-BOC-prolinol]-5,10-dioxo-3,4,5,10-tetrahydro-1-H-naphtho [2,3-C] pyran-3-yl) ketone BCH-2067

(1S, 2'S, 3R) and (1R, 2'S, 3S)-methyl-(1-[O-prolinol]-3,4,5,12-tetrahydronaphto-[2,3-C] pyran-3-yl) ketone hydrochloride salt (BCH-1658)

(1'-S, 1-R, 3-S) and (1'-S, 1-S, 3-R)-3-cyano-1-[2',3',6'-trideoxy-3'-trifluoroacetamido-4'-hydroxy-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-C] pyran-3-yl (BCH-1688)

(1'-S, 1-S, 3-R) and (1'-S, 1-R, 3-S)-methyl-(1-[2',3',4',6' tetradeoxy-3'-trifluoroacetamido-4'-O-methane-sulfonyl-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10 tetrahydronaphtho-[2,3-c] pyran-3-yl) ketone BCH-2095

(1'-S, 1-S, 3-R)-methyl-(1-[2',3',4',6' tetradeoxy-3'-trifluoroacetamido-4'-O-(2-bromo-acetyl)-L-lyxopyranose]-5, 10-dioxo-3,4,5,10 tetrahydronaphtho-[2,3-c] pyran-3-yl) ketone BCH-2105

(1'-S, 1-R, 3-S)-methyl-(1-[2',3',4',6' tetradeoxy-3'-methoxy-4'-O-methanesulfonyl-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10 tetrahydronaphtho-[2,3-c] pyran-3-yl) ketone BCH-2070

(1-S, 3-R) and (1-R, 3-S)-methyl-(1-(1-methoxy-4-oxocyclohexyloxy)-5,10-dioxo-3,4,5,10 tetrahydronaphto-[2,3-c] pyran-3-yl) ketone BCH-2096

(1R, 3S)-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-hydroxy-1,5-dihydro-L-lyxohexopyranose-2-yl)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c] pyran BCH-2144

(1S, 3R)-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-hydroxy-1,5-dihydro-L-lyxohexopyranose-2-yl)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c] pyran BCH-2145

(1'S, 1R, 3S)-5,10-dioxo-3-methoxymethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran (BCH-1691)

(1'S, 1S, 3R)-5,10-dioxo-3-methoxymethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho [2,3-c] pyran (BCH-1693)

(1'S, 1R, 3R)-5,10-dioxo-3-ethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c] pyran (BCH-2026)

(1'S, 1S, 3S)-5,10-dioxo-3-ethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran (BCH-2020)

(1'S, 1S, 3S)-5,10-dioxo-3-ethyl-1-(2',3',6'-trideoxy-3'-amino-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran (BCH-2021)

Trans-5,10-dioxo-1-acetamido-3-ethyl-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran (BCH-2027)

3-ethyl-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphto-[2,3-c] pyran (BCH-2154)

(1'S, 1R, 3S)-5,10-dioxo-3-isopropyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran (BCH-2053)

(1'S, 1S, 3R)-5,10-dioxo-3-isopropyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran (BCH-2052)

(trans)-5,10-dioxo-3-isopropenyl-1-methoxy-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran (BCH-2148)

(1'S, 1R, 3S)-5,10-dioxo-3-isopropenyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphto-[2,3-c]-pyran (BCH-2153)

(1'S, 1S, 3R)-5,10-dioxo-3-isopropenyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphto-[2,3-c]-pyran (BCH-2152)

(1'S, 1R, 3S)-5,10-dioxo-3-methoxycarbonyl-1-(2',3',6',trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyrano (BCH-2128)

(1'S, 1R, 3S)-isopropyl-[1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyranyl]-ketone (BCH-2112)

(1'S, 1R, 3S)-5,10-dioxo-3-isopropoxycarbonyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran (BCH-2122)

(1'S, 1S, 3R)-5,10-dioxo-3-isopropoxycarbonyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran (BCH-2121)

(1'S, 1S)-5,10-dioxo-3,3-dimethoxymethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexo-pyranose)-isochroman (BCH-1697)

(1'S, 1R, 4R)-5,10-dioxo-4-ethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c] pyran (BCH-2091)

(1'S, 1R, 3S)-5,10-dioxo-3-phenyloxymethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c] pyran (BCH-2032)

(1'S,1S,3S) and (1'S,1-R,3-R)-3-([2',3',6'-trideoxy-3'-trifluoroacetamido-4'-hydroxy-L-lyhohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphto-[2,3-c]-pyran-3-yl)-propene (BCH-2031)

(1'S,1-R,3-R)-3-([2',3',6'-trideoxy-3'-trifluoroacetamido-4'-hydroxy-L-lyhohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphto-[2,3-c]-pyran-3-yl)-propene (BCH-2163)

(1'-S,1-R,3-S)-3-([2',3',6'-trideoxy-3'-trifluoroacetamido-4'-hydroxy-L-lyhohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-c]-pyran-3-yl)-propene (BCH-1649)

(1'S,1S,3R) and (1'-S,1-R,3-S)-3-([2',3',6'-trideoxy-3'-trifluoroacetamido-4'-hydroxy-L-lyhohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-c]-pyran-3-yl)-propene (BCH-1648)

(1'-S,1-R,3-S,4a-S,10a-S)-methyl-(1-[2',3',4',6'-tetradeoxy-3'-methoxy-4'-O-methanesulfonyl-L-lyxohexopyranose)-4a,10a-epoxy-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-c] pyran-3-yl) ketone (BCH-2141)

(1'-S,1-S,3-R,4a-R,10a-R)-methyl-(1-[2',3',4',6'-tetradeoxy-3'-methoxy-4'-O-methanesulfonyl-L-lyxohexopyranose)-4a,10a-epoxy-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-c] pyran-3-yl) ketone (BCH-2149)

(1S,3R,1'S,5'S,6'S) and (1R,3S,1'S,5'S,6'S)-methyl-(1-[4'trifluoroacetamido-5'-methyltetrahydropyranyl]-5,10-dioxo-3,4,5,10-tetrahydronaphthaleno-[2,3-c] pyran-3-yl) ketone (BCH-1673)

(1'S,1S,3R)-3 (oximoethyl)-5,10-dioxo-1 (2,3,6-trideoxy-3-trifluoroacetamido-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c] pyran BCH-2101

(1'S,1R,3S)-3(oximoethyl)-5,10-dioxo-1 (2,3,6-trideoxy-3-trifluoroacetamido-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran BCH-2115

(1'ε,1S,3R)-3-(trifluoroacetamidoethyl)(-5,10-dioxo-1-(2',3','-trideoxy-3',4'-dihydroxy-L-lyxohexopyranose)=-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran (BCH-2018)

(1'R,1R,3S)-3-aceto-5,10-dioxo-1-(2-deoxy-2-chloroethyl-nitrosoureido-D-glucopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]pyran (BCH-2038)

3-Aceto-5,10-dioxo-1-methoxy-5,19-dihydro-1H-naphtho-[2,3-c]-pyran (BCH-2129)

(1R,3S) and (1S,3R)-3-aceto-5,10-dioxo-1 (4-chloroethylnitrosoureido cyclohexyl-oxy)-3,4,5,10tetrahydro-1H-naphtho-[2,3-c]-pyran (BCH-2114)

1-methoxy-3-N-anilinylcarbonyl-5,10-dioxo-5,10-dihydro-1H-naphtho-[2,3-c]-pyran (BCH-2044)

1-methoxy-3-(3-N-pyrrolidinomylpropylaminocarbonyl)-5,10-dioxo-5,10-dihydro-1H-naphtho-[2,3-c]-yran (BCH-2166)

(3-N-hydrochloroimidazolylpropyl)-1-methoxy-5,10-dioxo-5,10-dihydro-1H-naphtho-[2,3-c]-pyran-3-carboxamide (BCH-2157)

3-ethylthiocarbonyl-5,8-dioxo-1,3,4,5,10-pentahydro-naphtho-[2,3-c]-pyran (BCH-2003)

3-(5'-tosyloxazolyl)-5,10-dioxo-1,3,4,5,10-pentahydro-naphtho-[2,3-c]-pyran (BCH-2155)

(1'S,1S,3R)-1-(3'-trifluoroacetamido-2',3',6'-trideoxy-lyxo-L-hexopyranose)-3-methoxycarbonyl-3-methyl-3,4,5,10-tetrahydro-5,10-dioxo-naphtho-[2,3-c]-pyran (BCH-2076)

Methyl (1-methoxy-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho[2,3-c]pyran-3-yl) formate (BCH-2043)

1-Methoxy-5,10-dioxo-5,10-dihydro-1H-naphtho[2,3-c]pyran-3-carboxylic acid (BCH-2161)

(1,3-trans)-1-methoxy-3-carboxyl-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran (BCH-2045)

(1,3-cis)-1-methoxy-3-carboxyl-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran (BCH-2119)

(1,3-trans)-1-methoxy-3-N-anilinylcarbonyl-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran (BCH-2041)

(1,3-cis)-1-methoxy-3-N-anilinylcarbonyl-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran (BCH-2042)

(1'S,1R,3S)-2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose-3-[5'-tosyloxazolyl]-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran (BCH-2150)

(1'S,1S,3R)-2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose-3-[5'-tosyloxazolyl]-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran (BCH-2151)

(1,3-trans)-1-methoxy-3-(3'-aminothiazolyl)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran (BCH-1616)

(1,3-trans)-1-methoxy-3-dimethoxyphosphonoacetyl-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran (BCH-1674)

(1'S,1R,3S)-1-(3'-trifluoroacetamido-2',3',6'-trideoxy-L-lyxohexopyranose)-5,10-dioxo-4,5,10-trihydro-1H-naphtho-[2,3-c]-pyran (BCH-2077)

(1'S,1S,3R)-1-(3'-trifluoroacetamido-2',3',6'-trideoxy-lyxo-L-hexopyranose)-3-acetyl-3-methyl-3,4,5,10-tetrahydro-5,10-dioxo-naphtho-[2,3-c]-pyran (BCH-2082)

(1'S,1S,3R)-1-(3'-trifluoroacetamido-2',3',6'-trideoxy-lyxo-L-hexopyranose)-3-dimethoxyphosphonoacetyl-3,4,5,10-tetrahydro-5,10-dioxo-naphtho-[2,3-c]-pyran (BCH-1690)

(1'S,1S,3S)-1-(3'-trifluoroacetamido-2',3',6'-trideoxy-lyxo-L-hexopyranose)-3-methoxy-carbonyl-3-methyl-3,4,5,10-tetrahydro-5,10-dioxo-naphtho-[2,3-c]-pyran (BCH-2081)

(1'S,1S,3S)-1-(3'-trifluoroacetamido-2',3',6'-trideoxy-lyxo-L-hexopyranose)-3-dimethoxyphosphonoacetyl-3,4,5,10-tetrahydro-5,10-dioxo-naphtho-[2,3-c]-thiopyran (BCH-2037.001)

(1'S,1R,3R)-1-(3'-trifluoroacetamido-2',3',6'-trideoxy-lyxo-L-hexopyranose)-3-dimethoxyphosphonoacetyl-3,4,5,10-tetrahydro-5,10-dioxo-naphtho-[2,3-c]-pyran (BCH-2127)

(1'S,1S,3S)-1-(3'-trifluoroacetamido-2',3',6'-trideoxy-lyxo-L-hexopyranose)-3-acetyl-3-methyl-3,4,5,10-tetrahydro-5,10-dioxo-1H-naphtho-[2,3-c]-pyran (BCH-2090)

(1'S,1R,3S)-1-(3'-trifluoroacetamido-2',3',6'-trideoxy-lyxo-L-hexopyranose)3-dimethylphosphonoacetyl-3,4,5,10-tetrahydro-5,10-dioxo-naphtho-[2,3-c]-pyran (BCH-1689)

(1'S,1R,3S)- methyl-(1-[2',6'-dideoxy-3',4'-dihydroxy-2'-iodo-L-lyxohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphtho [2,3-c]-pyran-3-yl) ketone (BCH-2015)

(1'S,1R,3S)-methyl-(1-[2',6'-dideoxy-3'-4'-diacetoxy-2'-iodo-L-lyxohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphtho [2,3-c]-pyran-3-yl) ketone (BCH-1666)

(1'S,1S,3R)-methyl-(1-[2',6'-dideoxy-3',4'-diacetoxy-2'-iodo-L-lyxohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphtho [2,3-c]-pyran-3-yl) ketone (BCH-1667)

(1'S,1S,3R)-methyl-(1-[2',6'-dideoxy-3',4'-dihydroxy-2'-iodo-L-lyxohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphtho [2,3-c]-pyran-3-yl)-ketone (BCH-2014)

(1'S,1R,3S)-methyl-(1-[2',6'-dideoxy-3',4'-diacetoxy-2'-bromo-L-lyxohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-c]-pyran-3-yl) ketone (BCH-2100)

(1'S,1S,3R)-methyl-(1-[2',6'-dideoxy-3',4'-diacetoxy-2'-bromo-L-lyxohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-c]-pyran-3-yl) ketone (BCH-2099)

(1'S,1R,3S)-methyl-(1-[2',3',6'-trideoxy-2'-iodo-3'-trifluoroacetamido-4'-hydroxy-L-lyxohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-c]-pyran-3-yl) ketone (BCH-2023)

(1'S,1S,3R)-methyl-(1-[2',3',6'-trideoxy-2'-iodo-3'-trifluoroacetamido-4'-hydroxy-L-lyxohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-c]-pyran-3-yl) ketone (BCH-2022)

(1'S,1R,1S) and (1'S,1S,3R)-methyl-(1-[2',6'-dideoxy-3',4'-diacetoxy-2'-iodo-L-arabino-hexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-c]-pyran-3-yl) ketone (BCH-2065)

(1'S,1S,3R) and (1'S,1R,3S)-methyl-(1-[dideoxy-2',6'-dihydroxy-3',4'-L-lyxohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-c]-pyran-3-yl) ketone (BCH-2117)

(1'S,1S,3R) and (1'S,1R,3S)-methyl-(1-[dideoxy-2',6'-diacetoxy-3',4'-L-lyxohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-c]-pyran-3-yl) ketone (BCH-2118)

(1'S,1S,3R)-methyl-(6 and 9-hydroxy-1-[2',3',6'-trideoxy-3'-trifluoroacetamido-4'-hydroxy-L-lyxohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-c]-pyran-3-yl-ketone (BCH-2078)

Methyl-(1-O-[2'-piperidinemethanol]-5,10-dioxo-3,4,5,10-tetrahydronaphthaleno-[2,3-c] pyran-3-yl) ketone, racemic, hydrochloride (BCH-2069)

(1R,3S,1'S) and (1S,3R,1'S)-Methyl-(1-[2',3',4',6'-tetradeoxy-3',4'-bis-trifluoroacetamido-L-arabinohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphthaleno-[2,3-c] pyran-3-yl) ketone (BCH-2104 and BCH-2102)

(1R,3S,1'S) and (1S,3R,1'S)-Methyl-(1-[2',3',4',6'-tetradeoxy-3',4'-bis-trifluoroacetamido-L-arabinohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphthaleno-[2,3-c] pyran-3-yl) ketone (BCH-2047)

Methyl-(1-O-[N-BOC-3-piperidinemethanol]-5,6-dioxo-3,4,5,10-tetrahydronaphthaleno-[2,3-c] pyran-3-yl) ketone, mixture of isomers (BCH-2060)

Methyl-(1-O-[3-piperidinemethanol]-5,10-dioxo-3,4,5,10-tetrahydronaphthaleno-[2,3-c] pyran-3-yl) ketone hydrochloride salt, mixture of isomers (BCH-2061)

(1R,3S,1'S) and (1S,3R,1'S)-Methyl-(1-[2',3',4',6'-tetradeoxy-3',4'-bis-trifluoroacetamido-L-arabinohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphthaleno-[2,3-c] pyran-3-yl) ketone (BCH-2104)

(1S,3R,1'S)-Methyl-(1-[2',3',4',6'-tetradeoxy-3',4'-bis-trifluoroacetamido-L-arabinohexopyranose]-

5,10-dioxo-3,4,5,10-tetrahydronaphthaleno-[2,3-c] pyran-3-yl) ketone (BCH-2102)

72. A compound according to Claim 1 selected from the group consisting of:

(1'S, 1R, 3S)-5,10-dioxo-3-methoxycarbonyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran.

Methyl (1,5,8-trimethoxy-isochroman-3-yl) formate

Methyl (1-Methoxy-5,8-dioxo-5,8-dihydro-isochroman-3-yl) formate

(1S,2'S,3R,5'S) and (1R,2'S,3S,5'S)-1-[O-N-BOC-Serine-Leucine-Me ester]-3-aceto-5,8-dimethoxy-isochroman

(1S, 2'S, 3R) and (1R, 2'S, 3S)-1-[O-serine methyl ester]-3-aceto-5,8-dimethoxy isochroman.

(1S, 2'S, 3R) and (1R, 2'S, 3S)-1-[O-N-BOC-prolinol]-3-acetyl-5,8-dimethoxy isochroman

1-hydroxy-3-cyano-5,8-dimethoxy isochroman

1-hydroxy-3-cyano-5,8-dioxo-5,8-dihydroisochroman

(1'S, 1S, 3R) and (1'S, 1R, 3S)-5,10-dioxo-3-cyano-1-(2',3',6',-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1-H-naphtho-[2,3-c] pyran

5,8-Dimethoxy-3-(propane-2-one)-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-isochroman

5,8-Dioxo-3-(propane-2-one)-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-isochroman

(1R, 3S) and (1-S, 3R)-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzyloxy-1,5-dihydro-L-lyxohexo-pyranose-2-yl)-5,8-dimethoxy-3-acetoisochroman

(1R, 3S)-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzyloxy-1,5-dihydro-L-lyxohexopyranose-2-yl)-5,8-dioxoisochroman

(1S, 3R)-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzyloxy-1,5-dihydro-L-lyxohexopyranose-2-yl)-5,8-dioxoisochroman

(1'S, 1R, 3S)-5,8-dioxo-3-methoxymethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexo-pyranose)-5,8-dihydroisochroman

(1'S, 1R, 3S) and (1'S, 1S, 3R)-5,8-dioxo-3-methoxymethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexo-pyranose)-5,8-dihydroisochroman

(1'S, 1R, 3R)-5,8-dimethoxy-3-ethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-isochroman

(1'S, 1R, 3R)-5,8-dioxo-3-ethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-isochroman

(1'S, 1S, 3S)-5,8-dioxo-3-ethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexo-pyranose)-5,8-dihydro-isochroman

(trans)-1-acetamido-5,8-dioxo-3-ethyl-5,8-dihydro-isochroman

(1'S, 1R, 3S) and (1'S, 1S, 3R)-5,8-dioxo-3-isopropyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-5,8-dihydro-isochroman (40:60)

(1'S, 1S, 3R)-5,8-dioxo-3-isopropyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-5,8-dihydro-isochroman (40:60)

(1'S, 1S, 3R)-5,8-dimethoxy-3-isopropenyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexo-pyranose) isochroman.

(1'S, 1R, 3S)-5,8-dimethoxy-3-isopropenyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose) isochroman.

(1'S, 1R, 3S) and (1'S, 1S, 3R)-5,8 dimethoxy-3-methoxycarbonyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-isochroman.

(1'S, 1R, 3S) and (1'S, 1S, 3R)-5,8 dioxo-3-methoxycarbonyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-5,8-dihydro-isochroman.

isopropyl-(5,8-dimethoxy-isochroman-3-yl)-ketone

5,8-dimethoxy-3-isopropoxycarbonyl-isochroman

5,8-dimethoxy-3,3 bis (dimethoxymethyl)-isochroman

(1'S, 1S)-5,8-dimethoxy-3,3-dimethoxymethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-isochroman

(1'S, 1S)-5,8-dioxo-3,3-dimethoxymethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-isochroman

(1'S, 1R, 4R)-5,8-dimethoxy-4-ethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexo-pyranose)-isochroman

(1'S, 1S, 4S)-5,8-dimethoxy-4-ethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexo-pyranose)-isochroman

(1'S, 1R, 4R)-5,8-dioxo-4-ethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-isochroman

(1'S, 1R, 3S)-5,8-dimethoxy-3-phenyloxymethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-isochroman

(1'S, 1R, 3S)-5,8-dioxo-3-phenyloxymethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-isochroman

5,8-dimethoxy-3-(2-propenyl)-isochroman

(1'S,1S,3S) and (1'S,1-R,3-R)-1-(2',3',6',-trideoxy-3'-trifluoroacetamido-4'-O-paranitrobenzoyl-L-lyxohexopyranose)-5,8-dimethoxy-3-(2-propenyl)-isochroman

(1'S,1-R,3-R)-1-(2',3',6',-trideoxy-3'-trifluoroacetamido-4'-O-paranitrobenzoyl-L-lyxohexopyranose)-5,8-dimethoxy-3-(2-propenyl)-isochroman

(1S,3R-3(oximoethyl)-1 (2,3,6-trideoxy-3-trifluoroacetamido-4-p-nitrobenzoyl-L-lyxohexopyranose)-5,89-dimethosy-isochroman

(1R,3S)-3-(oximoethyl)-1 (2,3,6-trideoxy-3-trifluoroacetamido-4-p-nitrobenzoyl-L-lyxohexopyranose)-5,8-dimethoxy-isochroman

3-(Trifluoroacetamido-ethyl)-5,8-dimethoxy isochroman

(1S',1S,3R)-3-(trifluoroacetamidoethyl)-5,8-dimethoxy-1-(2',3',5'-trideoxy-3',4'-dihydroxy-L-lyxohexopyranose)-isochroman

(1'R,1R,3S)-3-aceto-5,8-dimethoxy-1(2-deoxy-2-chloroethylureido-3,4,6-triacetyl-D-glucopyranose)-isochroman

(1'R,1R,3S)-3-aceto-5,8-dimethoxy-1(2-deoxy-2-chloroethylureido-4,6-benzylidene-D-glucopyranose)-isochroman

(1R,3S) and (1S,3R)-3-Aceto-1 (4-chloroethylureido-cyclohexyloxy)-5,8-dimethoxy-isochroman

3-ethylthiocarbonyl-5,8-dimethoxy-isochroman

3-ethylthiocarbonyl-5,8-dioxo-1,3,4,5,8-penta-1H-benzo-[2,3-c]-pyran

3-(5'-tosyloxazolyl)-5,8-dimethoxy isochroman

3-(5'-tosyloxazolyl)-5,8-dioxo-1,3,4,5,8-pentahydrobenzo-[2,3-c]-pyran

(1'S, 1S, 3R)-1-(2',3',6'-trideoxy-I,3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-5,8-dimethoxy-3-aceto-3-methyl isochroman

(1'S,1S,3R)-1-(4'-p-nitrobenzoyl-3'-trifluoroacetamido-2',3',6'-trideoxy-lyxohexopyranose)-3-methoxy-carbonyl-3-methyl-5,8-dioxo-4,5,8-trihydro-1H-benzo-[2,3-c]-pyran

3-(5'-tosyloxazolyl)-5,8-dimethoxy isochroman

(1'S,1R,3S)-1-(4'-p-nitrobenzoyl-2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3-(5"-tosyloxazolyl)-5,8-dimethoxy isochroman

(1'S,1S,3R)-1-(4'-p-nitrobenzoyl-2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3-(5"-tosyloxazolyl)-5,8-dimethoxy isochroman

(1'S,1S,3R)-1-(4'-p-nitrobenzoyl-2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3-(5"-tosyloxazolyl)-5,8-dioxo-3,4,5,8-tetrahydrobenzo-[2,3-c]-pyran

(1'S,1S,3R)-1-(4'-p-nitrobenzoyl-2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3-(5"-tosyloxazolyl)-5,8-dimethoxy isochroman

(1'S,1S,3R)-1-(4'-p-nitrobenzoyl-2',3',6'-trideoxy-3'-trifluoroacetamido-L-lyxohexopyranose)-3-(5"-tosyloxazolyl)-5,8-dioxo-3,4,5,8-tetrahydrobenzo-[2,3-c]-pyran

(1'S,1S,3S)-1-(4'-p-nitrobenzoyl-3'-trifluoroacetamido-2',3',6'-trideoxy-lyxohexopyranose)-3-methoxy-carbonyl-3-methyl-5,8-dimethoxy-isochroman

(1'S,1R,3R)-1-(4'-p-nitrobenzoyl-3'-trifluoroacetamido-2',3',6'-trideoxy-L-lyxohexopyranose)-3-methoxy-carbonyl-3-methyl-5,8-dimethoxy-isochroman

(1'S,1R,3S)-1-(4'-p-nitrobenzoyl-3'-trifluoroacetamido-2',3',6'-trideoxy-L-lyxohexopyranose)-3-methoxy-carbonyl-3-methyl-5,8-dimethoxy-isochroman

(1'S,1R,3R)-1-(4'-p-nitrobenzoyl-3'-trifluoroacetamido-2',3',6'-trideoxy-L-lyxohexopyranose)-3-methoxy-carbonyl-3-methyl-5,8-dimethoxy-isochroman

(1'S,1R,3S)-1-(4'-p-nitrobenzoyl-3'-trifluoroacetamido-2',3',6'-trideoxy-lyxohexopyranose)-3-methoxy-carbonyl-3-methyl-5,8-dioxo-4,5,8-trihydro-1H-benzo-[2,3-c]-pyran

(1'S,1S,3S)-1-(4'-p-nitrobenzoyl-3'-trifluoroacetamido-2',3',6'-trideoxy-lyxohexopyranose)-3-methoxy-carbonyl-3-methyl-5,8-dioxo-4,5,8-trihydro-1H-benzo-[2,3-c]-pyran

(1'S,1S,3S) and (1'S,1R,3R)-1-(4'-p-nitrobenzoyl-3'-trifluoroacetamido-2',3',6'-trideoxy-L-

lyxohexopyranose)-3-acetyl-5,8-dimethoxy-thioisochroman

(1'S,1S,3S) and (1'S,1R,3R)-1-(4'-p-nitrobenzoyl-3'-trifluoroacetamido-2',3',6'-trideoxy-L-lyxohexopyranose)-3-acetyl-5,8-dioxo-4,5,8-trihydro-1H-benzo-[2,3-c]-pyran

(1'S,1S,3S) and (1'S,1S,3R)-1-(4'-p-nitrobenzoyl-3'-trifluoroacetamido-2',3',6'-trideoxy-L-lyxohexopyranose)-3-acetyl-3-methyl-5,8-dimethoxy-isochroman

(1'S,1S,3R)-1-(4'-p-nitrobenzoyl-3'-trifluoroacetamido-2',3',6'-trideoxy-L-lyxohexopyranose)-3-acetyl-3-methyl-5,8-dimethoxy-isochroman

(1'S,1S,3S) and (1'S,1S,3R)-1-(4'-p-nitrobenzoyl-3'-trifluoroacetamido-2',3',6'-trideoxy-lyxohexopyranose)-3-acetyl-3-methyl-5,8-dioxo-4,5,8-trihydro-1H-benzo-[2,3-c]-pyran

(1'S,1S,3R)[1'S,1R,3S]-5,8-dimethoxy 1(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-p-nitrobenzoyl-L-lyxohexopyranose)-3-dimethylphosphonoacetyl isochroman

(1'S,1S,3R)[1'S,1R,3S]-1-(2',3',6'-trideoxy-3'-trifluoro-acetamido-4'-p-nitrobenzoyl-L-lyxohexopyranose)-3-dimethylphosphonoacetyl-3,4,5,8-tetrahydronaphthaleno-[2,3-c]-pyran

(1'S,1S,3R) - 2,5-Dimethoxy-1-(2',6'-dideoxy-3',4'-diacetoxy-2'-iodo-L-lyxohexopyranose)-3-acetoisochroman

(1'S,1R,3S)-5,8-Dimethoxy-3-aceto-1-(2',6'-dideoxy-2'-iodo-L-lyxohexopyranose)-isochroman

(1'S,1R,3S)-3-aceto-1-(2',6'-dideoxy-2'-iodo-L-lyxohexopyranose)-5,8-dioxo-5,8-dihydroisochroman

(1'S,1R,3S)- 5,8-Dioxo-3-aceto-1-(2',6'-dideoxy-3',4'-diacetoxy-2'-iodo-L-lyxohexopyranose)-5,8-dihydroisochroman

(1'S,1S,3R)-5,8-Dioxo-3-aceto-1-(2',6'-dideoxy-3',4'-diacetoxy-2'-iodo-L-lyxohexopyranose)-5,8-dihydroisochroman

(1'S,1S,3R)-5,8-Dimethoxy-3-aceto-1-(2',6'-dideoxy-2'-iodo-L-lyxohexopyranose)-isochroman

(1'S,1S,3R)-3-aceto-1-(2',6'-dideoxy-2'-iodo-L-lyxohexopyranose)-5,8-dioxo-5,8-dihydroisochroman

(1'S,1R,3S) and (1'S,1S,3R)-2,5-Dimethoxy-1-(2',6'-dideoxy-3',4'-diacetoxy-2'-bromo-L-lyxohexopyranose)-3-acetoisochroman

(1'S,1S,3R)-2,5-Dimethoxy-1-(2',6'-dideoxy-3',4'-diacetoxy-2'-bromo-L-lyxohexopyranose)-3-acetoisochroman

(1'S,1R,3S)-5,8-dioxo-1-(2',6'-dideoxy-3',4'-diacetoxy-2'-bromo-L-lyxohexopyranose)-5,8-dihydroisochroman

(1'S,1R,3S)-5,8-dioxo-3-aceto-1-(2',6'-dideoxy-3',4'-diacetoxy-2'-bromo-L-lyxohexopyranose)-5,8-dihydroisochroman

(1'S,1R,3S) and (1'S,1S,3R)-2,5-Dimethoxy-3-aceto-1-(2',3',6'-trideoxy-2'-iodo-3'-trifluoroacetamido-4'-O-acetyl-L-lyxohexopyranose)-isochroman

(1'S,1S,3R)-2,5-Dimethoxy-3-aceto-1-(2',3',6'-trideoxy-2'-iodo-3'-trifluoroacetamido-4'-O-acetyl-L-lyxohexopyranose)-isochroman

(1'S,1R,3S)-5,8-Dimethoxy-3-aceto-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-2'-iodo-L-lyxohexopyranose)-isochroman

(1'S,1R,3S)-3-aceto-1-(2',3',6'-trideoxy -2'-iodo-3'-trifluoroacetamido-L-lyxohexopyranose)-5,8-dioxo-

5,8-dihydroisochroman

(1'S,1S,3R)-3-aceto-1-(2',3',6'-trideoxy-2'-iodo-3'-trifluoroacetamido-L-lyxohexopyranose)-5,8-dioxo-5,8-dihydroisochroman

(1'S,1S,3R) and (1'S,1R,3S)-5,8-Dimethoxy-3-aceto-1-(2',6'-dideoxy-3',4'-diacetoxy-2'-iodo-L-arabinohexopyranose) isochroman

(1'S,1R,3S)-5,8-Dimethoxy-3-aceto-1-(2',6'-dideoxy-3',4'-diacetoxy-2'-iodo-L-arabinohexopyranose) isochroman

(1'S,1R,3S) and (1'S,1S,3R)-3-aceto-1-(2',6'-dideoxy-2'-iodo-L-arabinohexopyranose)-5,8-dioxo-5,8-dihydroisochroman

(1'S,1S,3R) and (1'S,1R,3S)-5,8-dimethoxy-3-aceto-1-(2',6'-dideoxy-3',4'-diacetoxy-L-lyxohexopyranose) isochroman

(1'S,1S,3R) and (1'S,1R,3S)-5,8-dimethoxy-3-aceto-1-(2',6'-dideoxy-L-lyxohexopyranose) isochroman

(1'S,1S,3R) and (1'S,1R,3S)-5,8-dioxo-3-aceto-1-(2',6'-dideoxy-L-lyxohexopyranose)-5,8-dihydroisochroman

(1'S,1S,3R) and (1'S,1R,3S)-5,8-dioxo-3-aceto-1-(2',6'-dideoxy-3',4'-diacetoxy-L-lyxohexopyranose) isochroman

3-aceto-5,8-dioxo-3,4,5,8-tetrahydro-1H-benzo-[2,3-c]-pyran

1-O-[N-BOC-4-piperidinemethanol]-3-acetyl-5,8-dimethoxy isochroman racemic

(1R,3S,1'S) and (1S,3R,1'S)-Methyl-(1-[2',3',4',6'-tetradeoxy-3',4'-bis-trifluoroacetamido-L-arabinohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphthaleno-[2,3-c] pyran-3-yl) ketone

1-O-[N-BOC-3-piperidinemethanol]-3-acetyl-5,8-dimethoxy isochroman, mixture of isomers

(1'S,1R,3S) and (1'S,1S,3R) - 2,5-Dimethoxy-1-(2',6'-dideoxy-3',4'-diacetoxy-2'-iodo-L-lyxohexopyranose)-3-acetoisochroman

73. A compound according to claim 1 selected from the group consisting of :

Methyl (1-methoxy-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho[2,3-c]pyran-3-yl) formate

Methyl (1-methoxy-5,10-dioxo-5,10-dihydro-1H-naphtho[2,3-c]pyran-3-yl) formate

1-Methoxy-5,10-dioxo-5,10-dihydro-1H-naphtho[2,3-c]pyran-3-carboxylic acid

(1S, 2'S, 3R) and (1R, 2'S, 3S)-methyl-(1-[O-N-BOC-serine methyl ster]-5,10-dioxo-3,4,5,10-tetrahydro-1-H-naphtho [2,3-C] pyran-3-yl) ketone.

3,3 bis (methoxycarbonyl)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c] pyran

(1R,3S) and (1S,3R)-3-Aceto-5,10-dioxo-1 (4-chloroethylureido cyclohexyl-oxy)-3,4,5,10-tetrahydro-1H-nahtho-[2,3-c]-pyran

(3-N-imidazolylpropyl)-1-methoxy-5,10-dioxo-5,10-dihydro-1H-naphtho-[2,3-c]-pyran-3-carboxamide

(1's,1S,3R)-1-(4'-p-nitrobenzoyl-3'-trifluoroacetamido-2',3',5'-trideoxy-lyxohexopyranose)-3-methoxy-carbonyl-3-methyl-5,10-dioxo-4,5,10-trihydro-1H-naphtho-[2,3-c]-pyran

(1'S,1R,3S)-1-(4'-p-nitrobenzoyl-3-trifluoroacetamido-2',3',6'-trideoxy-L-lyxohexopyranose)-3-(5"-tosyloxazolyl)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran

(1'S,1S,3R)-1-(4'-p-nitrobenzoyl-3-trifluoroacetamido-2',3',6'-trideoxy-L-lyxohexopyranose)-3-(5"-tosyloxazolyl)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran

1-methoxy-3-acetyl-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran

3-bromoacethyl-1-methoxy-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran

Methyl-(6-hydroxy-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-c]-pyran-3-yl) ketone and methyl-(9-hydroxy-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-c]-pyran-3-yl) ketone (BCH-2062)

3-aceto-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran

3-bromoacetyl-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran

3-(3'-aminothiazolyl)-5,10-dioxo-1,3,4,5,10-pentahydro-naphtho-[2,3-c]-pyran

74. A compound according to claim 1 selected from the group consisting of:

5,10-Dioxo-3-(propane-2-one)-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexo-pyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c] pyran

(1R, 3S)-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzyloxy-1,5-dihydro-L-lyxohexopyranose-2-yl)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho [2,3-c] pyran

(1S, 3R)-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzyloxy-1,5-dihydro-L-lyxohexopyranose-2-yl)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c] pyran

(1'S, 1R, 3S)-5,10-dioxo-3-methoxymethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexo-pyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran

(1'S, 1S, 3R)-5,10-dioxo-3-methoxymethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexo-pyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran

(1'S, 1R, 3R)-5,10-dioxo-3-ethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c] pyran

(1'S, 1S, 3S)-5,10-dioxo-3-ethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexo-pyranose)-3,4,5,10-tetrahydro-1H-naphto-[2,3-c]-pyran

(1'S, 1S, 3R)-5,10-dioxo-3-isopropyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexo-pyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran

(1'S, 1R, 3S)-5,10-dioxo-3-isopropyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran

(1'S, 1R, 3S)-5,10-dioxo-3-isopropenyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexo-pyranose) 3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran

(1'S, 1S, 3R)-5,10-dioxo-3-isopropenyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexo-pyranose) 3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran

(1'S, 1R, 3S)-isopropyl-[1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-

lyxohexopyranose)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyranyl]-ketone

(1'S, 1R, 3S), and (1'S, 1S, 3R)-5,10-dioxo-3-isopropoxycarbonyl-1-(2',3',6'-trideoxy-3',trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran

(1'S, 1S, 3R)-5,10-dioxo-3-isopropoxycarbonyl-1-(2',3',6'-trideoxy-3',trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran

(1'S, 1S)-5,10-dioxo-3,3-dimethoxymethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c] pyran

(1'S, 1R, 4R)-5,10-dioxo-4-ethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran

(1'S, 1R, 3S)-5,10-dioxo-3-phenyloxymethyl-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c] pyran

(1'S,1S,3S) and (1'-S,1-R,3-R)-3-([2',3',6'-trideoxy-3'-trifluoroacetamidoo-4'-paramitrobenzoyl-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-c]-pyran-3-yl)-propene

(1'-S,1-R,3-R)-3-([2',3',6'-trideoxy-3'-trifluoroacetamidoo-4'-paramitrobenzoyl-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-c]-pyran-3-yl)-propene

(1'-S,1-R,3-S)-methyl-(1-[2',3',6'-trideoxy-3'-trifluoroacetamido-4'-iodo-L-lyxohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphtho-[2,3-c]-pyran-3-yl)-ketone (BCH-1620)

(1'S,1S,3R) and (1'S,1-R,3-R)-3-([2',3',6'-trideoxy-3'-trifluoroacetamido-4'-hydroxy-L-lyhohexopyranose]-5,10-dioxo-3,4,5,10-tetrahydronaphto-[2,3-c]-pyran-3-yl)-propene

(1'R,1R,3S)(-3-aceto-5,10-dioxo-1-(2-deoxy-2-chloroethylureido-4,6-benzylidene-D-glucopyranose)-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]pyran

(1'S,1R,3S)-1-4'-p-nitrobenzoyl-3'-trifluoroacetamido-2',3',6'-trideoxy-lyxohexopyranose)-3-methoxy-carbonyl-3-methyl-5,10-dioxo-4,5,10-trihydro-1H-naphtho-[2,3-c]-pyran

(1'S,1S,3S)-1-(4'-p-nitrobenzoyl-3'-trifluoroacetamido-2',3',6'-trideoxy-lyxohexopyranose)-3-methoxy-carbonyl-3-methyl-5,10-dioxo-4,5,10-trihydro-1H-naphtho-[2,3-c]-pyran

(1'S,1S,3S)-1-(4'-p-nitrobenzoyl-3'-trifluoroacetamido-2',3',6'-trideoxy-L-lyxohexopyranose)-3-acetyl-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-thiopyran

(1'S,1R,3R) and (1'S,1S,3S)-1-(4'-p-nitrobenzoyl-3'-trifluoroacetamido-2',3',6'-trideoxy-L-lyxohexopyranose)-3-acetyl-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-thiopyran

(1'S,1S,3S) and (1'S,1S,3R)-1-(4'-p-nitrobenzoyl-3'-trifluoroacetamido-2',3',6'-trideoxy-lyxohexopyranose)-3-acetyl-3-methyl-5,10-dioxo-4,5,10-trihydro-1H-naphtho-[2,3-c]-pyran

(1'S,1S,3R)-1-(4'-p-nitrobenzoyl-3'-trifluoroacetamido-2',3',6'-trideoxy-lyxohexopyranose)-3-acetyl-3-methyl-5,10-dioxo-4,5,10-trihydro-1H-naphtho-[2,3-c]-pyran

(1'S,1R,3S)-1-(2',3',6'-trideoxy-4'-p-nitrobenzoyl-3'-trifluoro-acetamido-L-lyxohexo pyranose)3-dimethyl-phosphonoacetyl-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran

(1'S,1S,3R) and (1'S,1R,3S)-1-(2',3',6'-trideoxy-4'-p-nitrobenzoyl-3'-trifluoro-acetamido-L-lyxohexo

pyranose)3-dimethylphosphonoacetyl-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran

(1'S,1S,3R)-methyl-(6 and 9-hydroxy-1-(2',3',6'-trideoxy-3'-trifluoroacetamido-4'-O-p-nitrobenzoyl-L-lyxohexopyranose)-5,10-dioxo-3,4,5,10-tetrahydro-1H-naphtho-[2,3-c]-pyran-3-yl) ketone

75. A pharmaceutical composition according to claim 4 wherein said compound is combined with an agent facilitating targetting of said combination to tumor or cancer cells.

76. A pharmaceutical composition according to claim 69, wherein said agent is selected from the group consisting of monoclonal antibodies, polyclonal antibodies, proteins, and liposomes.

77. A pharmaceutical composition according to claim 71, wherein said agent is selected from the group consisting of monoclonal antibodies, polyclonal antibodies, proteins, and liposomes.

78. A method of treatment of tumors or cancer said method comprising the step of administering to an animal, a therapeutically effective amount of at least one compound according to claim 1.

79. A method for the treatment of tumors or cancer said method comprising the step of administering to an animal, a therapeutically effective amount of at least one compound or combination of clinically defective antitumor agents according to claim 2.

80. A method according to claim 79, wherein said animal is a mammal.

81. A method according to claim 80, wherein said mammal is a human.

INTERNATIONAL SEARCH REPORT

Inter nal Application No
PCT/CA 93/00463

A. CLASSIFICATION OF SUBJECT MATTER
IPC 5 C07H17/00 C07H17/04 C07D311/92 C07D311/76 C07D335/08
C07D221/06 A61K31/70 A61K31/35 A61K31/38 A61K31/435

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 5 C07H C07D A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	PATENT ABSTRACTS OF JAPAN vol. 11, no. 349 (C-456) 14 November 1987 & JP,A,62 120 379 (HOECHST JAPAN KK) 1 June 1987	1-3,60, 61,78-81
Y	see abstract	1-38, 60-81
X	WO,A,91 19725 (IAF BIOCHEM INTERNATIONAL INC) 26 December 1991 cited in the application	72
Y	see the whole document	1-38, 60-81
Y	EP,A,0 475 473 (PHARMACHEMIE BV) 18 March 1992 cited in the application see page 6 - page 7; claims	1-38, 60-81
	-/--	

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
25 March 1994	07. 04. 94

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax (+31-70) 340-3016	Day, G

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	TETRAHEDRON LETTERS., vol.32, no.39, 1991, OXFORD GB pages 5279 - 5282 SINGH S.B. ET AL 'Structure and Stereochemistry of Thysanone: A Novel Human Rhinovirus 3C-Protease Inhibitor from Thysanophora penicilloides' see page 5280 ---	1-4,13, 20
X	JOURNAL OF THE CHEMICAL SOCIETY, PERKIN TRANSACTIONS 1, 1990, LETCHWORTH GB pages 2163 - 2174 ALDERSLEY M.F. ET AL 'Pyridinium Ylides in Syntheses of Napthopyrandiones and in Regioselective Synthese of Acylated Anthraquinones Related to Fungal and Bacterial Metabolites' see page 2164 ---	1,3,26, 28
X	JOURNAL OF ANTIBIOTICS., vol.29, no.7, July 1976, TOKYO JP pages 704 - 709 HOEKSEMA H. AND KRUEGER W.C. 'Kalafungin. II Chemical Transformations and the Absolute Configuration' see page 705 ---	1,3,26
X	JOURNAL OF ANTIBIOTICS., vol.44, no.1, January 1991, TOKYO JP pages 103 - 107 DEVYS M. AND BARBIER M. '6-O Demethyl-5-Deoxyfusabarin and its Anhydro Derivative produced by a mutant of the fungus Nectria Haematocca blocked in Fusarabin biosynthesis' see page 103 ---	1,3,26, 28
X	JOURNAL OF THE CHEMICAL SOCIETY, CHEMICAL COMMUNICATIONS., 1981, LETCHWORTH GB pages 534 - 535 CHORN T.A. ET AL 'Synthese of Naphtho[2,3-c]pyran-5,10-quinines using Cerium Ammonium Nitrate' see the whole document -----	1,2

INTERNATIONAL SEARCH REPORT

I national application No.
PCT/CA93/00463

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Remark: Although claims 78-81 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [ ] Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. [ ] As all searchable claims could be searches without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

information on patent family members

Inter nal Application No
PCT/CA 93/00463

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
WO-A-9119725	26-12-91	AU-A-	8097391	07-01-92
		CN-A-	1058781	19-02-92
		EP-A-	0533744	31-03-93
EP-A-0475473	18-03-92	NL-A-	9001834	16-03-92
		CA-A-	2048510	17-02-92
		JP-A-	4297486	21-10-92